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Volume 234 JANUARY 24, 1946 Number 4

HODGKIN'S DISEASE*

VII. Treatment and Prognosis

HENRY JACKSON, JR., M.D.,† AND FREDERIC PARKER, JR., M.D.‡

BOSTON

THIS concluding paper of the series on various aspects of Hodgkin's disease concerns treatment and prognosis.

TREATMENT

Hodgkin's Paragranuloma

It is difficult to give advice on the treatment of Hodgkin's paragranuloma. In view of the apparently localized nature of the disease in many cases and the excellent results of surgery in 2 of our cases, it seems reasonable to advocate radical dissection, followed by irradiation whenever the condition seems to be sharply confined to a readily accessible region. It must be pointed out, nevertheless, that there have been recurrences in 3 of 5 cases in which surgical excision was practiced, and this fact indicates that excision should be followed by prophylactic irradiation. Of the 2 patients who have been subjected to this routine, one is alive and entirely free from signs or symptoms thirty-four years after the onset of her disease, and the other, having remained symptom-free for twenty-four years, developed Hodgkin's granuloma and died three years later. If radical dissection does not appear to be warranted, fairly heavy doses of x-ray are indicated provided that not more than one area is involved.

Hodgkin's Granuloma

There is no specific treatment for Hodgkin's granuloma, nor is there likely to be one until its cause has been found. There are, however, a number of therapeutic measures that may be expected to prolong life and that will certainly alleviate the symptoms, often for a long period of time.

Three points should be borne in mind. First, in the great majority of cases, by the time the patient is first seen the disease has affected more than one organ. Second, virtually every organ and tissue may be involved sooner or later, and the utmost diligence must be exercised by the clinician to discover as early as possible any involvement of internal organs, so that appropriate therapeutic measures may be promptly instituted. Third, the disease may begin insidiously in an isolated and localized focus, and it is in all probability a circumscribed process at onset. This at least is our opinion, although we recognize that it is not shared by many students of the subject. In short, we believe that Hodgkin's granuloma has its origin in a single isolated focus, often, unfortunately, internal, and spreads insidiously, although rather rapidly, eventually involving many organs.

It is thus clear that if one is to have any hope of actually curing the condition, it must be discovered in its earliest stages and be promptly treated with the utmost energy. It is equally clear that both the clinician and the radiologist must constantly be on the lookout for evidence of involvement of internal organs, and must not content themselves with the gratifying results of treatment directed solely to superficial lymph nodes, which are in most cases merely the visible expression of an internal lesion. This point has become increasingly obvious in recent years.

A biopsy should be performed prior to therapy in all cases in which it is feasible. Unless this is done, and unless the removed lymph node is properly fixed and stained, one cannot be certain of the diagnosis, nor can the ultimate results of any form of therapy be accurately judged. Furthermore, a careful and complete physical examination, together with routine blood studies and x-ray examination of the chest, should be done in all cases at the first visit. Additional x-ray or laboratory studies may be indicated in specific cases.

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This is the seventh and concluding article of a series of seven papers covering the various aspects of Hodgkin's disease.

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The most valuable therapeutic measure is irradiation. On this point all are agreed, but there is no consensus concerning the best method of applying it. Indeed, it is clear that in a disease showing such diverse and protean manifestations and running such an unpredictable and variable course, this is almost inevitable. The treatment must necessarily be adapted to the individual patient; the results of therapy can be adjudged only over a long period of time and with due regard to the varied manifestations of the disease.

There are various schools of thought regarding the proper type of irradiation, and one may choose for oneself that which seems the most logical, the most promising and the most suitable.

Gilbert[1] has covered this entire subject with care, and to his article the reader is especially referred. A partisan of high-voltage x-ray, he advocates wide irradiation of the regions patently invaded as well as those suspected of invasion, and contends that it is essential to irradiate widely enough to be reasonably certain of subjecting the entire involved regions to the action of the rays. In consequence of his belief that local recurrences begin in granulomatous islands subjected to inadequate irradiation, his initial doses are relatively large. Panteleoroentgen therapy is, in his opinion, of more harm than good.

His therapeutic regime is briefly as follows. Diagnosis is made by biopsy whenever feasible. Involved areas and regions suspected of being involved by reason of the symptoms are irradiated, from 180 to 200 kilovolts being used through portals up to 20 by 20 cm. To each area are given fractional doses of approximately 200 r every other day until the desired total has been delivered — a minimum total depth dose of 500 r to each focus. The paravertebral, para-aortic and retroperitoneal nodes are irradiated if general signs, such as fever, pruritus and asthenia, persist after successful irradiation of apparently localized disease elsewhere. Treatment is renewed only if evidence of recurrence is seen.

Sixteen of Gilbert's 52 patients treated in this manner were still alive at the time of his report; of these, 9 (17 per cent of the total) had survived five years or more and 3 had survived for ten years or more.

In recent years, our own therapeutic approach has been similar to that of Gilbert. A 250-kilovolt machine is used. Each area involved or suspected of being involved is treated through a portal of sufficient size to embrace the entire field, in fractionated doses until the required amount has been given. It is probably best to give comparatively small doses to any given area if the disease is widespread, but many authorities believe that large, heavy doses should be given if the condition appears to be confined to one region. No further irradiation is resorted to unless there is a recurrence.

Recently, we have in certain selected cases used a supervoltage (1000-kilovolt) x-ray machine. It is too early to come to any conclusion concerning the relative merits of this method of irradiation. All patients are seen at frequent intervals, — two weeks to three months, — and great diligence is exercised in attempting to discover, by one means or another, any new focus of disease. Any persistent symptom or sign not explainable on other grounds is regarded as being due to Hodgkin's granuloma and appropriate irradiation is given. This is an important part of the treatment, irrespective of the exact type of irradiation used. Of the 35 patients in our series still alive on January 1, 1945, 17 (49 per cent) have survived for five years or more. Thus, 16 per cent of the patients in the entire series who were subjected to systematic treatment and adequately followed survived for five years or more.

It is our belief that the internist and the radiologist should care for the patient conjointly and that all details of x-ray therapy should be left to the radiologist. No matter what type of x-ray therapy is used, — and it is obvious that competent authorities advise varying methods of attack, — certain practical points should be borne in mind.

Extremely large mediastinal masses must be treated with great caution, for not infrequently they are extremely radiosensitive, in which event too rapid destruction by excessive amounts of x-ray may result in the organism's being flooded with products of necrosis, which may bring about highly toxic manifestations or even death.

The acute form of Hodgkin's granuloma, accompanied by high temperatures, an elevated white-cell count and the signs and symptoms of an acute infection, must be treated with great care and conservatism. A rapid rise in temperature calls for temporary cessation of therapy. The situation is somewhat analogous to that seen in acute leukemia.

The presence of active tuberculosis contraindicates irradiation of the lungs and mediastinum in the usual doses, as does renal insufficiency, especially if associated with nitrogen retention.

The presence of unexplained fever, vague gastrointestinal disturbances, fleeting abdominal pains, generalized itching or a persistently elevated white-cell count, with an increase of polymorphonuclear leukocytes, usually indicates the presence of diseased lymph nodes deep in the abdomen or in the para-aortic region, and irradiation of these areas often causes a remission of the symptoms.

We have been increasingly impressed with the wisdom of relentless treatment even in the face of what appear to be overwhelming odds. Of course a point is reached when further irradiation is fruitless and even harmful, but this does not usually occur until after many courses of treatment, and it is remarkable what may be accomplished in the relatively early stages of the disease even though

the patient may seem at the time to be at death's door. Many patients have rapidly and markedly failed, only to return to comparative health when hospitalized, transfused and given appropriate irradiation. Gilbert[1] cites such a case from his own practice.

To obtain the best co-operation and thus the best results, it is wise to give the patient a general idea of what may be expected of x-ray therapy. It is not necessary to name the disease; it would obviously be unwise to picture the final outcome, and it is unnecessary to dwell on details. It is, however, proper to point out that the outward manifestations of the disease will diminish or even disappear, but with a warning that the same disease process may subsequently reappear in another place and that any untoward sign or symptom should be immediately reported. Only thus and by repeated routine examination can one hope to keep the disease in abeyance.

The question of marriage and pregnancy is, of course, of great importance. Both should probably be advised against, but, as Gilbert says, "these events occur in spite of us." If pregnancy should take place, it is necessary to decide whether it should be terminated. This question cannot be categorically answered. Three of our patients have become pregnant. One, a multipara, was aborted at her own request. She was alive and free from symptoms three years later. The other two, both primiparas, gave birth to normal babies, and each was well one and two years later, respectively, both children remaining well. Gilbert has had a similar although more extensive experience. The ultimate fate of the offspring cannot, of course, be foretold, but the present data seem to justify allowing pregnancy to go to term provided that one or both of the parents realize the potentialities.

In assigning to the fundamental disorder signs and symptoms that may properly be attributed to it, enthusiasm must be tempered with a modicum of knowledge of general medicine. One of our patients, a sixty-year-old Armenian, with "small Latin and less Greek" said that he was unable "to pass the water." What more tempting, in view of the fact that his disease was widely disseminated, than to see as a cause of this complaint a granulomatous process in the prostate and to irradiate that organ. Forthwith, he was indeed, "unable to pass the water." It was with much relief and some chagrin that we witnessed a complete and lasting disappearance of his symptoms following a prostatectomy for the simple, benign prostatic hypertrophy of old age.

In almost all early publications concerning irradiation, it was stated that although the symptoms could thus be alleviated, life could not be prolonged. It has recently become increasingly apparent that this is not the case. We agree with Gilbert and others that the average duration of survival is prolonged. In 1923, Desjardins and Ford[4] found that only a scant 10 per cent of their patients survived for more than five years. In 1932, Holfelder and Hummell (quoted by Gilbert[1]) reported that nearly 18 per cent of their patients had passed the five-year mark. In Gilbert's series, 34 per cent fell into this category.

The results of irradiation vary within wide and unpredictable limits; as a rule, they are fairly satisfactory. Generally speaking, however, bone lesions are less radiosensitive than are foci in other organs. Lesions of the sternum, however, usually show a satisfactory response. In any event, relief from pain is often striking, and in some cases bone regeneration and repair have been observed. That excellent results may be obtained in such cases is attested by the following case.

E. W., (P 1933), a 20-year-old man was admitted to the hospital on January 3, 1933. In September, 1931, he had noticed a "swollen gland" behind the left ear. One month later this became painful and other lymph nodes appeared in the left side of the neck. One of these was removed, and a diagnosis of Hodgkin's granuloma was made. During the next 5 years, lymph nodes appeared from time to time in the neck, axillas and groins, but always diminished or disappeared after appropriate high-voltage x-ray treatment. In addition, the patient was periodically troubled by intense generalized itching, which was partially controlled by spray x-ray treatment and by viosterol in large doses. His general health, however, continued to be good, and he remained mentally and physically active.

In June, 1936, the patient complained of pain, especially on motion, in the lower lumbar region. This was relieved by the administration of 60r by spray to the body anteriorly and 100 r posteriorly. In October of that year there were no palpable lymph nodes, and the patient's general condition was excellent, — although he had lost some weight, — but he complained of intense pain in the lumbar region, particularly on the right side.

Physical examination showed a marked lumbar scoliosis on the left side and intense contraction of the lumbar spinal muscles on the right side. X-ray films showed a destructive process of the bodies and transverse processes of the 1st and 2nd lumbar vertebras. There was a slight degree of vertebral collapse. Six hundred roentgens was given over the involved area, and the pain completely disappeared. In January, 1937, there was some return of the pain but complete relief was again obtained after the administration of 400r to the lumbar region.

In May, 1937, the patient again complained of considerable discomfort in the lumbar region, and x-ray examination showed an increase of the destruction of the 1st and 2nd lumbar vertebras. Nine hundred roentgens was given over the involved area, and in October there was evidence that new bone was being laid down in the bodies of the vertebras and that fingerlike processes of new bone were reaching out into the soft tissue to bridge the existing defect. The radiologist noted that there appeared to have been an arrest of the process and a laying down of calcium deposits in the ligamentous structures surrounding the lateral portions of the 1st and 2nd lumbar vertebras on the left.

The general result was that in spite of the bony destruction there was a partial and fairly effective ankylosis of the spine. Nine hundred roentgens more was given, and the patient continued to be in reasonably good health and was able to control the discomfort in the lumbar region by salicylates. In spite of the marked bone lesion he was able to swim, play tennis and ski, although he complained, with a smile, that a left hand telemark was hard to accomplish.

By October, 1939, the lesion of the lumbar spine had extended to include the body of the 12th dorsal vertebra. There was, however, no increase in symptoms, and the patient was still active in athletics 8 years after the initial symptoms

and 3 years after the demonstration by x-ray of a destructive process in the spine involving at least three vertebras. Early in 1940 there developed considerable pain in the lower back and in both legs, which gradually increased in severity and could be controlled only by opiates. The patient remained cheerful, however, and his physical activities were limited solely by the pain, which became so severe in the fall of 1940 that a dorsal cordotomy was performed. The operation was entirely successful in so far as relieving the pain was concerned, but the patient failed rapidly and died in December, 9 years after the initial symptoms.

In addition to irradiation, three therapeutic adjuvants must be considered: blood transfusions, general care and surgery.

Some authors object to transfusions and believe that they are rarely of benefit and may even be harmful (Wallhauser[5]). We,[1] on the contrary, agree with Gilbert that they are of inestimable value, and it is doubtful whether the reactions to which some authors have drawn attention would occur if careful attention were paid not only to the group but also to the subgroup of both donor and recipient. This is particularly important if repeated transfusions are necessary at rather long intervals; for although, for instance, A_1B_1 blood may produce no reaction on the first transfusion in an A_1B_1 recipient, the patient may gradually build up antibodies against B_1 in such a manner that subsequent transfusions even from the same donor are accompanied by violent reactions.[6] It is our custom to transfuse patients whose red-cell count is 3,000,000 or below unless they are in the terminal stages of the disease. We have never seen an untoward reaction when the bloods were properly matched in both the major and the minor agglutinations.

Iron in the form of ferrous sulfate may be of benefit.

It is obvious that general care is of importance in any chronic condition, and this is no less so in Hodgkin's granuloma. Plenty of rest, ample food that is high in vitamins and the other essential elements, fresh air and sunlight within the tolerance of the patient are all of real value. Not a few patients volunteer the statement that their sense of well-being is greatly enhanced if they stay out-of-doors in the sun.

Obvious foci of infection should be removed, for they undoubtedly have a provocative influence on the condition. For itching, in addition to the irradiation referred to above, local applications of 0.5 per cent phenol in olive oil may be tried. For pain, particularly that arising from bone lesions, salicylates in full doses often produce surprisingly good results. One of our patients had a destructive lesion of the lumbar spine associated with marked pain. X-ray therapy brought about a regression of the bone lesion, but the pain, which was apparently dependent on the resulting scoliosis and muscle spasm, persisted. For several years it has been controlled by large doses — 2 to 6 gm. — of aspirin a day, and the patient is able to live a normal and indeed active life.

Our experience with cordotomy for pain has been most unsatisfactory, although there are no doubt cases in which it is of benefit. In 1 case, the skillful injection of the posterior roots with alcohol was followed by complete relief of pain. There was no further discomfort until the patient's death a year later.

The question of surgical intervention is a moot one. First championed by Yates and Bunting in 1917,[7] it has since fallen into disrepute. The great majority of writers on the subject have concluded that it is useless, some because they have seen it fail again and again, others because they have seen the rapid return of lymph nodes in the operative field, and still others because of their belief that Hodgkin's granuloma is always a generalized disease from the start — a belief for which there are no valid grounds. It is true that by the time the patient first seeks medical advice, the process is usually widespread or at least inoperable. It is also true that in many cases the original focus is internal and therefore inaccessible, but both clinical experience and autopsy findings tend to show that the disease begins in one focus and spreads from it — slowly in some cases and rapidly in others.

Gilbert writes: "Surgical procedures have shown themselves useless; they do not influence the evolution of the disease. Local recurrence or extension develops shortly after operation, except in the benign, local and peripheral forms in which the lymph nodes are still movable." Baker and Mann[4] adopt a somewhat more militant and optimistic attitude. They cite the first and second cases in their series, in each of which there was performed surgical excision of the diseased tissues, associated with deep x-ray therapy. The first patient was alive and well thirteen years and the second eleven years after operation. It is the opinion of these authors that when the lymph-node enlargement is localized, surgical excision should be practiced and the area subsequently irradiated. We share this view, with the full recognition that suitable cases are indeed rare and that even in them some hidden focus not apparent at the time of operation may frustrate attempts at cure. Much has been said and written about the necessity for early diagnosis in cancer, and it is generally appreciated that in early recognition of this disease lies the best hope of true cure. The same can be said for Hodgkin's granuloma.

Two of our patients with this disease have been subjected to radical excision of cervical lymph nodes. One was alive and free from signs and symptoms of disease ten years after operation, and the other is alive and well seven years after operation. Both patients were children. It is obvious that in view of the extremely variable course of the disease, no conclusions can be drawn from these cases, and at best the results are only suggestive. Too often, however, one hesitates, argues and procrastinates

until the time comes when it can be truthfully said that operative interference is uncalled for. Too often one waits to see what will happen. Too seldom does one proceed radically. Such is the early history of many incurable diseases. The paradox is that when the lymphadenopathy is still possibly amenable to complete surgical removal, it is liable to be regarded as benign, whereas when it has become inoperable, one contents oneself by saying that it always has been so.

Certain authors have claimed excellent therapeutic results with Hodgkin's granuloma, confined to the gastrointestinal tract, but so far as our experience goes, these patients fare badly, for in no case did a patient survive for more than eighteen months after the initial symptoms, and the average duration of life from onset to death was only nine months. Patients with gastrointestinal lesions incidental to a generalized process similarly appear to have an unfavorable prognosis, if the figures derived from such a small series may be regarded as significant.

The psychologic aspects of treatment should never be overlooked. If the patient is a physician, he should be told the precise diagnosis. The details of the treatment and prognosis need not, and indeed should not, be dwelt on. We have cared for a considerable number of doctors afflicted with Hodgkin's disease or allied conditions, and all but one have borne their disease with cheerful stoicism from beginning to end. In the single exceptional case, serious family difficulties unquestionably contributed to the patient's mental undoing.

If the patient is a layman, it is probably best not to name the disease, even though — as is usually the case — one is asked what it is. Practically all patients are content with evasive answers, and rarely press the point if they are casually told that some lymph nodes are enlarged for some obscure reason and that much can be done to alleviate their symptoms. The mere assurance that symptomatic improvement can be achieved almost always sets the patient's mind at comparative ease, and the initial therapeutic success tends to tide him over subsequent recurrences, even though these may be less amenable to such therapeutic measures as are available. As time passes, the patient himself often comes to the realization that he is going to have the disease the rest of his life, and this recognition gradually changes to an awareness that he is sure to die of the disease. This inner awakening to the bitter truth hurts far less than would a blunt statement on the part of the attendant physician. Less frequently the patient imperceptibly — to himself — grows worse and worse, and he is never genuinely conscious of the impending end. Still less frequently sudden death occurs even when the patient appears to be doing well.

Very rarely one encounters a patient who asks how long he will live, and means it. In such cases an entirely plausible reason is always given for wishing this exact information. The absence of such a logical reason is usually sufficient evidence that the patient is not truly serious in his questioning. Even so, dogmatism must be avoided, the course of the disease is too erratic. For example, one young man asked how long he would live. From his former physician he had learned the diagnosis. When asked why he wished to know, he replied calmly that he wanted to plan his life in accordance with the prognosis. He was told that he would live for one year, and at his request he was shown the evidence on which this statement was based. "All right," he said, "I will build a house — that takes a year." Six years later, the physician who had made the prognosis received a note in which the patient remarked that the skiing was excellent in the mountains and invited him to come there for the weekend. The patient died four years later following a major surgical operation. The individual patient is not the average patient, and the rules of Hodgkin's disease are made to be broken.

It should be recognized that patients with this disease are unusually quick to grasp the significance of any remark arising from the physician's awareness that the end is approaching; indeed, they exaggerate it. In several of our cases, fear and despair has supplanted hope and a sense of security. For example, a patient who lived in a distant town had done unusually well for five years, but then began to fail, although without realizing it. It was suggested that he get in touch with a local physician so that there might be someone at hand who was familiar with his case. On reaching home he telephoned his son and said, "Well, my death warrant has been signed." In a week he was dead. It may be argued that he would have died anyway, but this is doubtful, and at least he would have died in peace had the subject been brought forward earlier and more tactfully.

In all cases some responsible member of the family, not necessarily the nearest of kin, must be told in lay terms the diagnosis and the probable prognosis. Even here, however, one must be cautious, for, as has been repeatedly said, each case is a law unto itself.

Hodgkin's Sarcoma

The treatment of choice in Hodgkin's sarcoma, as in other forms of Hodgkin's disease, is irradiation; yet it must be admitted that there is no convincing evidence that such treatment, even when given in full doses, is of much avail. Not infrequently, virtually no response is obtained, a result that in Hodgkin's granuloma is extremely rare. In the presence of anemia, transfusions are helpful. The fact that in most cases the condition arises in an internal organ or in the retroperitoneal lymph nodes and is thus less likely than otherwise to be diagnosed at an early stage militates still further against successful therapeusis.

If the condition is discovered at an early stage, when the lesion is comparatively localized, radical surgical intervention appears to be indicated, but we have not encountered any such case.

Prognosis

Hodgkin's Paragranuloma

For certain forms of malignant disease, such as osteogenic sarcoma, a maximal time of survival may be set with some degree of accuracy, and in the great majority of cases the physician may rest assured that an actual cure has been effected if the patient survives this date. This situation does not obtain in Hodgkin's paragranuloma.

The prognosis of this disease is comparatively good. Of 26 patients followed to date, 14 (54 per cent) have been alive and free from symptoms for five years or more, and 5 have survived a fifteen-year period (Table 1). It is of considerable significance that of the 12 patients who have died, 5 succumbed to diseases entirely unrelated to their disease; the remainder developed Hodgkin's granuloma and died in less than ten years after onset.

Table 1. *Survival Period in Cases of Hodgkin's Paragranuloma.*

Type of Case	Survival to Date or to Death	No. of Cases
	yr.	
Patient alive	Less than 3	0
	3–9	7
	10–24	6
	25 or more	1
Patient dead	Less than 3	5*
	3–9	6†
	10 or more	1
Total		26

*Death due to unrelated causes in 3 cases.
†Death due to unrelated causes in 2 cases.

Hodgkin's Granuloma

Hodgkin's granuloma is usually regarded as a fatal condition, leading to death in one to three years. In general such is the case; yet it is important to remember that the individual patient is not the average one, that the span of life from onset varies within wide limits, and that rarely a patient survives without evidence of active disease for so long a time that an actual cure may be considered at least possible.

Table 2. *Average Duration of Disease from Onset to Death according to Age at Onset in Cases of Hodgkin's Granuloma.*

Age at Onset	Median Duration	No. of Cases
yr.	yr.	
Less than 10	2.5	14
10–19	2.4	26
20–29	2.8	21
30–39	2.4	19
40–49	1.3	23
50–59	2.6	18
60–69	0.6	12
70–79	0.9	2
80–89	0.7	1
Total		136

In Table 2 is shown the duration of life from the first sign or symptom that could properly be considered as due to the disease itself in the 136 cases of our series in which the patients died of the disease after being followed throughout its course. Three patients died of entirely unrelated causes and are therefore not included. It is apparent that the average length of life from onset to death is approximately two and a half years. Uddströmer's[3] data, based in a like manner on 494 fatal cases, are in essential agreement with ours, and Wallhauser,[4] from a review of the literature, has come to essentially the same conclusions. These average figures, however, by no means tell the whole story. Thirteen per cent of our patients lived for five years or more after onset, and 1 died eleven years after onset (Table 3). About 30 per cent, therefore, lived definitely longer than either those in the average or median group, and 13 per cent lived twice as long.

Table 3. *Duration of Disease from Onset to Death in Cases of Hodgkin's Granuloma.*

Duration	Present Series (136 cases)	Uddstromer's Series (494 cases)
yr.	%	%
Less than 1	24	33
1–2	45	45
3–4	17	16
5–9	13	6
10 or more	1	0

When one considers those patients who were still alive, a somewhat different picture is seen (Tables 4 and 5). It is apparent that the duration of the disease in the patients in both series is notably longer than it was in those who died. Whether this is due to the statistical error of a relatively small series — 69 living cases — or can be attributed to the increased efficacy of more recent x-ray therapy is a question that cannot be answered with any degree of assurance. The fact remains, however, that of these 69 patients, 28 (40 per cent) had had their disease for five years or more and that an additional 6 per cent had survived a ten-year period.

Table 4. *Average Duration of Disease from Onset to Date according to Age at Onset in Cases of Hodgkin's Granuloma.*

Age at Onset	Median Duration	No. of Cases
yr.	yr.	
Less than 10	5.0	5
10–19	6.0	3
20–29	5.6	9
30–39	4.3	4
40–49	5.7	6
50–59	4.8	6
60–69	3.0	1
70–79	5.2	1
Total		35

Table 5. *Duration of Disease from Onset to Date in Cases of Hodgkin's Granuloma.*

Period	Present Series (35 cases)	Uddstromer's Series (34 cases)
yr.	%	%
Less than 3	22	9
3–4	28	47
5–9	44	38
10 or more	6	6

The question therefore naturally arises whether at the onset there are any criteria by which one can foretell the course of the disease. Fifteen of

our patients died in less than six months after the apparent onset, and 11 survived for eight years or more, 7 of these being alive and in reasonably good health for eight to twenty-two years after the first symptom.

If these two groups of cases, examples of the prognostic extremes, are contrasted, certain definite points stand out. The onset in the rapidly fatal cases was usually suggestive of an acute infection or indicated internal involvement. Chills, dyspnea, cough, fever, abdominal pain, sweating and dysphagia were seen at the very beginning of the disease, and only 7 of the 15 patients had palpable superficial lymph nodes when first seen, although all but two had peripheral lymphadenopathy prior to death (Table 6). In almost all cases in which cough, dyspnea, chills, sweats and fever were present at the onset of the disease, death occurred within six months. One cannot of course expect this rule to hold in every case, but it appears to be a helpful prognostic guide. As Uddströmer[9] points out, however, the disease process may have been in existence much longer than the symptoms indicate when it has its origin in the hilar, mesenteric or retroperitoneal lymph nodes, and the actual duration of the disease may therefore be longer than is evidenced by the available clinical data.

TABLE 6. *Most Frequent Initial Symptoms in Fifteen Rapidly Fatal Cases of Hodgkin's Granuloma.*

SYMPTOM	No. OF CASES
Cough	9
Dyspnea	7
Superficial lymphadenopathy	7
Chills	5
Hemoptysis	2
Fever	2
Dysphagia	1
Sweats	1

Of the 11 patients who survived for eight years or longer, and 8 of whom are now alive and in reasonably good health, 8 sought medical advice for simple, painless localized lymphadenopathy without any associated signs or symptoms. One had in addition a certain amount of general fatigue, 1 complained of dyspnea, and 1 entered the hospital for the first time with a complaint of weakness of the legs.

The contrast between these two groups is sufficiently arresting to demand attention. By and large, in the rapidly fatal cases there was an onset suggestive of an acute infection, whereas in those of long duration the patients presented themselves with simple lymphadenopathy, only occasionally associated with symptoms of generalized disease. The more nearly a given case approaches one or another of the extremes, the more does the course run true to form.

Most students of this subject agree that no definite relation exists between the onset of pulmonary findings and the progress of the disease. Falconer and Leonard[10] were unable to determine any connection between the time of onset of pulmonary symptoms and the time of death. It appears, however, that these authors dated the onset of pulmonary involvement from the first pulmonary symptoms, which may well have been due to mediastinal or hilar node involvement rather than to actual implication of the parenchyma. Similarly, Pierce et al.[11] state that the roentgenological appearance offers no criteria for prognosis.

Our own experience has been somewhat more definitive. No patient in whom pulmonary lesions were demonstrated at autopsy lived for more than eight months after these changes had been discovered during life, and the great majority died within three months. Three patients who gave x-ray evidence of pulmonary invasion from mediastinal or hilar nodes survived for over two years after the demonstration of these changes, but in no case was there autopsy confirmation of the reported pulmonary involvement. It is perhaps of some interest that all 3 of these patients had an unusually long course, averaging over eight years. No definite conclusions can therefore be drawn, but it seems probable that involvement of the lung parenchyma is associated in many cases with rapidly advancing disease.

Ziegler[12] concluded that Hodgkin's disease runs a more rapid course in children than in older patients. Uddströmer[9] believed the reverse to be true. Our own experience is that age alone has little or no influence on the prognosis.

That the disease may run an extremely rapid course has been already pointed out. For example a six-year-old girl was noted by her parents to have enlarged lymph nodes in each side of the neck in December, 1933, and one week later developed cough and fever. She died of respiratory failure on January 10, 1934, within six weeks of onset.

In sharp contrast is the following case.

A.P., a 10-year-old boy, in 1915 developed a painless lump in the left side of the neck. It gradually increased in size until November, 1917, when it was removed by surgery. Histologic examination of the node showed the typical picture of Hodgkin's granuloma (MGH-S17-11-58).

On admission to the hospital on December 17, 1917, physical examination was entirely normal except for the presence of several firm lymph nodes, varying from 0.5 to 1.0 cm. in diameter, in the anterior triangle of the right side of the neck. No lymph nodes were palpable in any other area. The red-cell, white-cell and differential counts were essentially normal.

Between December 27 and May 31, 1918, a total of 6100 mc. hr. of radium (2 mm. of lead and 2 cm. of gauze screening) was given to the left side of the neck and the left axilla, although there were no palpable lymph nodes in the latter area. The cervical lymph nodes disappeared, and the patient was not seen again until December 20, 1924. At that time he was in excellent condition, and the physical examination was entirely within normal limits.

He returned on August 22, 1930, when a 2-cm. node was found under the left jaw. There were many carious teeth in the lower jaw. The node was removed on September 6. The microscopic diagnosis was Hodgkin's granuloma. A full suberythema dose of x-ray was given at 250 kilovolts over the left side of the neck.

Since that time the patient has remained entirely well. When last seen in December, 1939, 22 years after onset,

he was free from symptoms and physical examination disclosed no abnormalities.

Between the extremes of these two cases lie the majority of cases. It is well to bear in mind that it is often difficult to predict the course with any degree of accuracy. That such is indeed the fact is well illustrated by a case in which the patient had at onset symptoms of a generalized disease and signs of involvement not only of lymph nodes but of bone, but was alive and at work twelve years later.

Rarely sudden death occurs. MacCallum[13] describes a case in which the patient leaned forward to drink a cup of tea and died instantly. Autopsy showed that the odontoid process of the axis had been completely destroyed by the disease and that the slight effort of motion had dislocated the spinal column so as practically to cut the cord in two. One of our patients, a boy of fifteen, was eating his luncheon in comparative comfort. In the midst of the meal, he sighed, laid down his knife and fork and expired. Permission for an autopsy was not obtained. As Wallhauser[5] points out, the manner and time of death depend on several variable factors, chiefly the course, — acute or chronic, — the organs and situations involved, the degree of anemia, secondary infections, the quality of the patient's resistance and the treatment. The importance of the last two factors is too frequently overlooked.

It is difficult to evaluate the prognostic significance of bone lesions in Hodgkin's disease. Many patients in our series so affected died within less than one and a half years of x-ray discovery of the lesion and 63 per cent died within less than a year after it. A patient with a massive erosion of the sternum, however, was in seemingly good health and hard at work twelve years after its discovery, and of the patients who died within a year of the demonstration of the bone lesion, 33 per cent had already had unequivocal signs of Hodgkin's disease elsewhere for three years or more. From the available evidence it does not appear that bone lesions materially alter the outlook. In this opinion Uehlinger[14] concurs.

Hodgkin's Sarcoma

None of our patients with Hodgkin's sarcoma lived for more than three years after onset, and nearly 60 per cent died within two years (Table 7).

TABLE 7. *Duration of Disease from Onset to Death in Cases of Hodgkin's Sarcoma.*

DURATION	NO. OF CASES
mo.	
1–6	12
7–12	6
13–24	13
25–36	1
Total	32

Again one sees the sharp contrast between Hodgkin's sarcoma and Hodgkin's granuloma. In our experience, the former is invariably fatal within a comparatively short period of time, whereas the latter usually runs a relatively benign course and in rare cases is actually cured.

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THE WOLFF–PARKINSON–WHITE SYNDROME

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TO THOSE with extensive electrocardiographic experience, especially if it includes a large proportion of young adults, the finding of the pattern of a short PR interval and a prolonged QRS complex comes as no great surprise. That it is not a rare occurrence, as might be concluded from the many papers in the literature reporting one or two cases, needs to be emphasized, because this combination is still all too frequently misinterpreted as being of clinical significance. Such misinterpretation might be considered negligible if the electrocardiographic findings occurred but rarely. On the other hand, if the pattern is as frequent as experience indicates, it becomes important, particularly in the military service, that it receive wider publicity.

During the routine interpretation of electrocardiograms in an Army general hospital, this curious pattern seemed to appear with greater frequency than had been expected. Accordingly, the last 2000 electrocardiograms were reviewed. The pattern of a short PR interval and a prolonged QRS complex was encountered at one time or other in 7 cases. Since the records represented 1356 patients, the incidence was 0.5 per cent. At the present strength of the armed forces this is equivalent to about four divisions. If even a small percentage of such men were to be returned from combat areas with diagnoses of bundle-branch block, a considerable loss of manpower would result. Furthermore, even when such a record is later accurately evaluated in another hospital, it is difficult and often impossible to salvage the patient because of a firmly entrenched cardiac neurosis or neurocirculatory asthenia. Moreover, when and if these patients are returned to civilian life, they will probably remain partially ineffective.

Brief summaries of these cases follow, together with an illustrative electrocardiogram.

CASE 1. A 19-year-old soldier was admitted to the hospital because of recurrent episodes of dizziness, shortness of breath, palpitation and occasional fainting. These symptoms had been present since infancy and were usually brought on by exertion. Early in life the patient had been cautioned about his heart because of a murmur. He was admitted to an overseas hospital, where a precordial systolic murmur was heard, and was evacuated with a diagnosis of interventricular septal defect and bundle-branch block.

Examination revealed an inconsequential precordial systolic murmur and an electrocardiographic pattern of a short PR interval and a prolonged QRS complex. The patient was made to exercise to the point of shortness of breath and dizziness, without any change in the blood pressure, cardiac rhythm or electrocardiographic pattern. The intravenous injection of 2 mg. of atropine sulfate also failed to alter the electrocardiogram. Fluoroscopic examination of the heart revealed no abnormalities. The patient was considered to have severe neurocirculatory asthenia.

CASE 2. A 34-year-old soldier entered the hospital because of attacks of paroxysmal tachycardia, which had begun 5 years previously. Between attacks he had been symptom-free. Physical and roentgenographic examinations were normal. Electrocardiograms consistently showed a short PR interval and a prolonged QRS complex, which were unaffected by atropine.

CASE 3. A 34-year-old soldier was admitted on his return from overseas with a diagnosis of rheumatic fever. He had had a probable attack of rheumatic fever at the age of 4 and an authenticated attack in an Army hospital in September, 1943. He was discharged back to duty and fared well until June, 1944, when he had a recurrence of joint pain, with fever and an elevated erythrocytic sedimentation rate. Several electrocardiograms were said to have revealed intraventricular conduction defect. The patient was evacuated to the United States, and on arrival had no complaints.

The physical examination was normal. Review of the previous electrocardiograms showed the pattern of a short PR interval and a prolonged QRS complex, but the record obtained on admission was normal save for a single beat, which was at first interpreted as a late ventricular ectopic beat. A review of the previous records made it apparent, however, that this beat was identical with the complexes previously present. Following the subcutaneous administration of 1 mg. of physostigmine, the pattern was reproduced in all cycles. There was no clinical or laboratory evidence of active rheumatic fever or of organic heart disease.

CASE 4. A 25-year-old soldier with a history of possible rheumatic fever at the age of 12 was admitted to an overseas hospital because of multiple-joint pain, without objective swelling, redness or local heat. There was no fever, leukocytosis, or elevation of the erythrocytic sedimentation rate. Electrocardiograms, however, were interpreted as showing left bundle-branch block. Largely on the basis of the latter report the patient was considered as having active rheumatic infection and was evacuated to the United States.

On admission there were multiple complaints, including fleeting joint pain, precordial pain, palpitation and shortness of breath. Physical, laboratory and roentgen-ray examinations were normal. Electrocardiograms, which were identical with previous records, showed the pattern of a short PR interval and a prolonged QRS complex. The patient was considered to have a psychoneurosis, including neurocirculatory asthenia and psychogenic "rheumatism." The electrocardiogram is reproduced in Figure 1.

CASE 5. The clinical record was not available in this case, but the final diagnosis was severe neurocirculatory asthenia.

CASE 6. A 30-year-old soldier was seen because of attacks of paroxysmal tachycardia for the last 4 years. In the intervals between attacks he was essentially symptom-free. Physical and roentgen-ray examinations of the heart were normal. The electrocardiogram showed a short PR interval and a prolonged QRS complex.

CASE 7. A 33-year-old soldier was referred for an electrocardiogram before shock therapy for catatonic schizophrenia. Although a history of sharp precordial pain and shortness of breath was obtained, the patients had no complaints and answered all leading questions in the affirmative. The history was accordingly discounted. Physical and roentgen-ray examinations of the heart were normal. The electrocardiogram revealed a short PR interval and a prolonged QRS complex. Shock therapy was not employed because of an erroneous diagnosis of bundle-branch block.

DISCUSSION

The mechanism of this curious electrocardiographic pattern, first clearly defined by Wolff, Parkinson and White,[1] still remains unexplained. The theory of a short-circuiting bundle between the auricles and ventricles, proposed by Wolferth and Wood,[2] has been almost universally accepted by recent authors. The demonstration by Butterworth and Poindexter[3, 4] that the pattern can be

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reproduced in animals by the artificial introduction of such a short circuit attests to the logic of the theory, but neither this experimental work nor the histologic demonstration of an auriculoventricular band in such a case by Wood, Wolferth, and Geckeler[5] absolutely establishes the mechanism.

There are several features of this syndrome that are not satisfactorily explained by the theory of an accessory auriculoventricular band. For example, the pattern apparently disappears with advancing age, yet vagal tone increases rather than decreases with age. Inasmuch as an increase in vagal tone may reproduce the pattern when the electrocardiogram is normal, as in Case 3, and a decrease in vagal tone produced by exercise or atropine may temporarily abolish it, it is curious that it is not more frequent in older people. Regular disappearance of the anatomic structure after a certain age seems unlikely.

A somewhat more important objection to the theory of an accessory band is to be found in the failure of multiple precordial leads to establish early excitation of one or the other ventricle. Figure 1 shows a series of CF leads in Case 4. It may be seen that the interval from the beginning of QRS complex to the onset of the intrinsic deflection — that is, the first rapid downward movement of the string — is the same — about 0.08 second — in leads taken from the right and the left precordial position. This feature distinguishes the precordial lead pattern from that of bundle-branch block, in which the interval between the onset of the QRS complex and the intrinsic deflection is prolonged over the blocked ventricle but is normal over the unblocked ventricle. Equal blocking over both ventricular areas, as seen in Figure 1, offers a serious objection to the theory

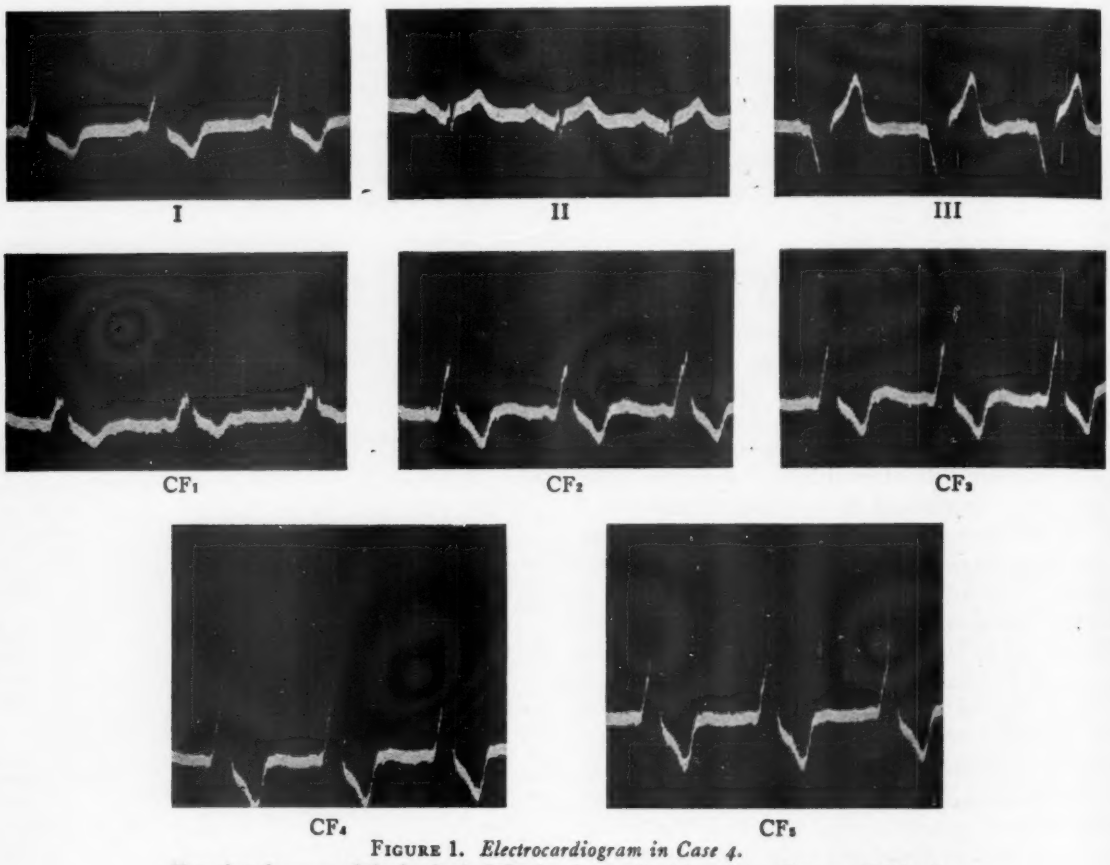

FIGURE 1. *Electrocardiogram in Case 4.*
Note that the onset of the intrinsic deflection is equally delayed in all precordial leads.

of abnormally early excitation of one of the ventricles.

The spread of impulses over the ventricles, if activation occurs by way of an accessory pathway, may logically be considered more comparable to ventricular ectopic beats than to bundle-branch block. The literature immediately available contained no information on the pattern of precordial leads during ventricular ectopic beats. Accordingly, multiple chest leads were obtained in patients with frequent ventricular ectopic beats. The result in one such case — that of a twenty-five-year-old Negro with trigeminal rhythm but no detectable heart disease — is shown in Figure 2. It may be seen that the pattern is the same as in left bundle-branch block. Over the right ventricle the onset of the intrinsic deflection in the ectopic beat is delayed for only 0.04 second — 0.02 second more than for the normal beats in the same area. Over the left side of the precordium the onset of the in-

trinsic deflection is delayed for 0.11 second in the ectopic beat, as compared with 0.04 second in the normal beats. The available material has not allowed exhaustive study of precordial leads, but at present it is fair to say that the chest leads in the

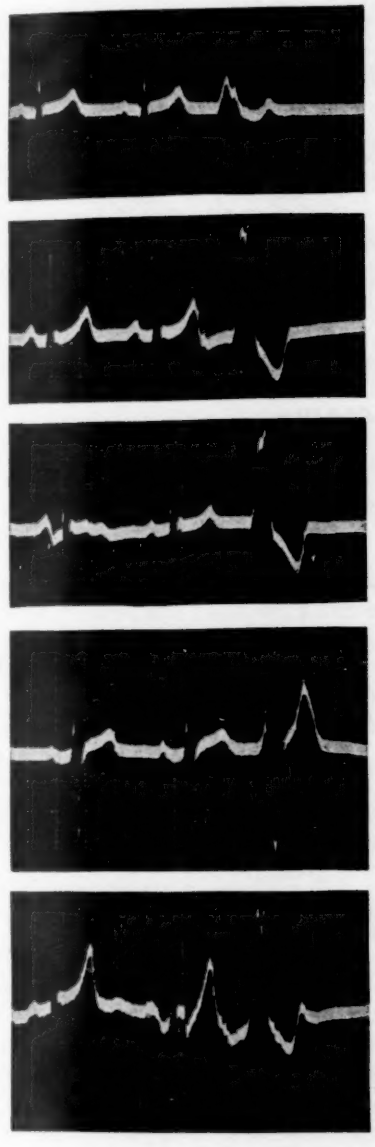

FIGURE 2. *Electrocardiogram Showing Trigeminal Rhythm Due to Regularly Recurring Ventricular Ectopic Beats.*
Note that the onset of the intrinsic deflection in the ectopic beats varies with the position of the precordial electrode, as it does in bundle-branch block.

Wolff–Parkinson–White pattern do not resemble those from either ventricular ectopic beats or bundle-branch block.

In the first clear clinical description of this pattern, that by Wolff, Parkinson and White[1] it was said to be usually associated with paroxysmal tachycardia. In the present series only 2 patients had clear-cut paroxysmal tachycardia, 1 had no symptoms, 3 had neurocirculatory asthenia, and 1 had schizophrenia, possibly with neurocirculatory asthenia. That the relatively high incidence of neurocirculatory asthenia is not explainable on the basis that it is such patients who, in this age group, are likeliest to have electrocardiograms made is attested by the fact that by far the majority of the 2000 records reviewed were made in patients in various stages of rheumatic fever. Only one patient (Case 3) was in the latter group, and he had no symptoms whatever.

Two explanations of the association of this electrocardiographic pattern and neurocirculatory asthenia are plausible. First, the deranged nervous system may actually produce the pattern. This theory is supported by the frequent, although by no means invariable, alteration from abnormal to normal or from normal to abnormal patterns induced by drugs known to act on the vegetative nervous system. Second, the abnormal sequence of excitation may result in cardiac sensations that, in certain susceptible persons, may lead to "heart consciousness," neurocirculatory asthenia or cardiac neurosis. Although the diagnosis of organic heart disease made on the basis of the electrocardiogram undoubtedly contributed to an increase in symptoms in the present group, it was not the cause of the symptoms of neurocirculatory asthenia, for the complaints in all the patients in whom this diagnosis has been made were present before the electrocardiogram was obtained.

The recent report of sudden death in a patient who had previously shown the Wolff–Parkinson–White pattern[5] should not lead to undue emphasis on the possibility of such a disaster. The rarity of sudden death in young persons without clear pathologic entities and the apparent frequency of the abnormal electrocardiographic pattern warrant accepting a slight risk, if such exists, to avoid creating or adding to anxiety states.

SUMMARY

The electrocardiographic pattern of a short PR interval and a prolonged QRS complex has been encountered rather frequently in an Army general hospital, the incidence being 0.5 per cent of patients in whom electrocardiograms were made. Several of these patients had been unnecessarily evacuated from combat areas.

Provided that this experience is not unique, it seems likely that many more soldiers will be unnecessarily evacuated unless those responsible for electrocardiographic interpretations familiarize themselves with the pattern and recognize its probable benignity. The frequency of psychoneurosis in the present series of patients was high, and particularly in such patients it is desirable to avoid adding to their symptoms with a diagnosis of bundle-branch block or myocardial damage.

The mechanism of this pattern is still unexplained. The theory of aberrant conduction tissue between

the auricle and ventricle does not satisfactorily account for some of the characteristics of the syndrome. In particular, it does not seem to explain observations made with multiple chest leads.

Since this manuscript was submitted, a comprehensive study of precordial, thoracic and esophageal leads in the Wolff–Parkinson–White syndrome has been reported by Rosenbaum et al.[6] They suggest that when the anomalous pattern is present, conduction occurs by way of *both* the normal conduction pathways and one or more accessory pathways. Although this suggestion helps to explain the pattern better than does the theory of aberrant spread throughout the ventricles, the hypothesis rests on a good deal of speculation. It is logical speculation, however, and tempts one to conjecture that the premature excitation involves a particular muscle bundle — probably one of the deeper ones. The reasons for such a conjecture are as follows: First, the magnitude of the premature component of the QRS complex suggests that a sizable bulk of muscle is involved. Second, if one assumes that the onset of the intrinsic deflection signals the arrival of the impulse at the epicardial surface underlying the electrode, it follows from the study of unipolar leads that the premature excitation does not reach the epicardial surface at any point that can be reached by indirect unipolar leads.

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SYNCOPE IN BLOOD DONORS

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THE present emergency has provided an unusually abundant opportunity for the study of syncope, or fainting, in blood donors. Although not in itself serious, fainting results in loss of time to the donor, it is detrimental to the efficiency of the donor center, and, as pointed out by Taylor,[1] an occasional donor has fallen and suffered injury. The present investigation of some of the clinical and etiologic aspects of syncope was undertaken to aid in reducing the incidence of fainting in blood donors. Aside from practical considerations, it is hoped that the observations and data recorded in this paper will shed some light on the pathogenesis of the complex and interesting problem of syncope, about which, as McDowell[2] has recently stated, there exists a great deal of confusion.

Material and Methods

This study concerns two series of blood donors bled under different circumstances and therefore offering some interesting comparative data. The first series consisted of 6882 donors — 2202 men and 4680 women — who were bled between May, 1942, and March, 1943. The blood was obtained at the Atlanta Red Cross Blood Donor Center under the direction of the Blood Research and Plasma Laboratory of the United States Army. Physically fit donors were selected on a basis similar to that of the present Red Cross requirements, with certain important variations. A donation could be either 250 or 500 cc., but no 500-cc. donations were taken from persons under twenty-one years of age or weighing less than 150 pounds. If a donor was nervous or if other reasons seemed to warrant it, only 250 cc. was taken even if the donor was within the weight and age limits of the larger donation. All the bleedings were done by the staff of physicians assigned to the center, and a closed-vacuum-bottle method was employed. The donations amounted to only thirty to seventy a day, so that it was possible to adopt an unhurried attitude and to permit the donor to rest for ten or fifteen minutes on the bleeding bed after the donation. The second series consisted of 9251 donors — 3917 men and 5334 women. Bleedings were taken from March 8 to June 1, 1943. This program was carried out according to the methods and technics recommended for use in Red Cross blood procurement centers.[1] All accepted donors weighing 110 pounds or over gave 500 cc. of blood, unless, as in exceptional cases, the bleeding had to be stopped before this amount was obtained. The technics of the preparation of the arm and the venipuncture were the same in both series, but in the second series the standard Red Cross bleeding set[1] was used, and practically all the bleedings were done by specially trained graduate nurses. One or two staff physicians were in charge of the bleeding room at all times. Of necessity, the atmosphere was somewhat more impersonal than in the first series; moreover, the rest after bleeding was shortened to five minutes unless otherwise indicated.

The personnel was instructed regarding the early signs and symptoms of syncope, and a trained nurse especially designated as the "reaction nurse"

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was available at all times in the bleeding room. In addition, all donors with syncope were seen by the medical officer in charge, and in each case a report stating the time of onset and giving various other data pertaining to the reaction was immediately made out. The pulse and blood pressure were taken at five-minute intervals and recorded until normal levels were obtained.

Classification of Syncope

Syncope is a transient form of vasomotor collapse that has certain characteristic symptoms and signs. Although various classifications have been proposed for syncope in blood donors,[3] reactions that did not require additional rest were disregarded in this study. Those in which there occurred loss of consciousness or convulsive manifestations were arbitrarily classified as severe syncope; otherwise the case was classified as mild syncope. In this manner 162 cases of syncope were encountered in the first series, 17 of which were severe, and 527 cases in the second series, 158 of which were severe.

On the basis of this experience an attempt has been made to present the clinical findings and to discuss the constitutional and contributory factors in syncope. Since the 158 cases of severe syncope in the second series were the best defined and most accurately controlled, more detailed observations are presented in regard to them than in regard to those in the first series.

Clinical Manifestations

The symptoms and signs of syncope encountered in this study were similar to those described in blood donors by Brown and McCormack.[4]

Symptoms

Syncope often developed without warning, but some donors complained of weakness or dizziness, and at times restlessness, yawning or sighing occurred. Rarely a definite aura was present. The most frequent symptom with the attack in the 158 severe cases in the second series was a feeling of warmth, which occurred in 63 per cent. Epigastric distress (32 per cent) and nausea (32 per cent) were also present but were usually mild in degree. In addition, there were a variety of other less frequent complaints, such as spots before the eyes, blindness, tinnitus, urgency to void or defecate and numbness and tingling in the hands.

Table 1. *Physical Signs of Severe Syncope.*

Physical Sign	Percentages
Pallor	99
Loss of consciousness	95
Fall in pulse	83
Fall in blood pressure	77
Sweating	65
Dilated pupils	38
Generalized convulsions	28
Vomiting	7
Loss of sphincter control	6
Hyperventilation	5
Tetany	4

Signs

The nature and frequency of the various physical signs of severe syncope are shown in Table 1.

Pallor. This was the most frequent sign and was usually marked. At times the skin showed a cyanotic tinge, and in some of the more profound cases the patient gave the appearance of impending death.

Loss of consciousness. The onset was usually abrupt. Most donors remained unconscious for only a few seconds, but in some unconsciousness was more prolonged. Consciousness was generally recovered suddenly, and there was amnesia for the event.

Fall in pulse. Of the 158 donors with severe syncope, 83 per cent had a pulse of 60 or lower. In a control group 4.5 per cent of donors had a pulse of 60 or below after bleeding. In cases of extremely severe syncope the pulse was frequently imperceptible or very slow.

Fall in blood pressure. Seventy-seven per cent of the donors with severe syncope had a drop in systolic blood pressure of 30 or more, compared with 1 per cent in a control group. There was always a concomitant and corresponding drop in the diastolic pressure. The lowest blood-pressure level was usually the initial one, and this did not necessarily occur during the period of unconsciousness. The blood pressure generally rose during the recovery period, which in most cases was half an hour or less, but occasionally the low blood pressure persisted for hours.

Sweating. This was a frequent finding. Drenching perspiration was observed more frequently in men, especially in those with profound syncope. Sweating occurred all over the body, but unlike this sign in traumatic shock, the skin was usually warm rather than cold.

Dilatation of pupils. Pupillary changes were found in over a third of the cases of severe syncope. These were of variable degree and often so transient that they may have been missed in some patients. Occasionally the pupils were constricted, but no definite correlation between either type of pupillary changes and the degree of syncope was noted.

Generalized convulsions. In donors who had convulsive seizures the onset was almost always abrupt. A tonic spasm was usually present throughout the body, and frequently the head and eyes deviated to one side, with the back arched in opisthotonos. The pupils were generally dilated and momentarily fixed. In some cases there were clonic movements of the extremities, followed by a period of snorting, stertorous respiration. The face was usually flushed and occasionally slightly cyanotic. The blood pressure during the attack was normal or slightly elevated. Immediately afterward in some donors a drop in blood pressure and pulse was observed, but in others there was no fall in blood pressure or pulse, either during or after a

convulsion. All these donors were apparently unconscious during the seizure, but none of them bit their tongues or sustained any significant injury, even with violent convulsions.

Vomiting. Although relatively infrequent, vomiting was occasionally severe and profuse. Many donors felt relieved after it, but in some cases nausea and epigastric distress persisted for hours. Vomiting may be an outstanding feature of otherwise mild cases of syncope.

Loss of sphincter control. Although of rare occurrence, urinary incontinence was observed, especially in young women. It was invariably associated with deep syncope and often occurred during or just following a convulsive seizure. Loss of bowel control was not observed, but a few donors experienced an urgent desire to defecate.

Hyperventilation and tetany. Various respiratory changes, such as slow, rapid, deep, shallow and intermittent breathing, were observed. Of these, hyperventilation was the outstanding finding. Following it the typical symptoms and signs of tetany were observed in 6 cases, with carpopedal spasm, a positive Chvostek sign and numbness, tingling and

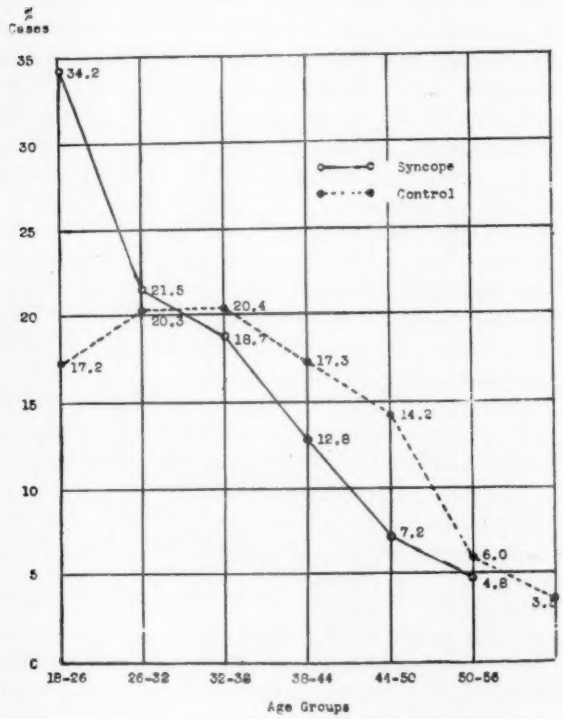

FIGURE 1. *Relation of Age to Syncope.*

pain in the jaw and extremities. One of these donors also presented evidence of syncope, although she did not lose consciousness.

Tetany may occur without syncope, but tetany, convulsions and syncope may all occur in the same person. Frazer and Forweather[5] recently described 7 cases of tetany in blood donors, in some of which there was a fall in blood inorganic phosphorus. This finding has not been confirmed by other investigators, however, and it is generally accepted that overbreathing in nervous persons with subsequent loss of carbon dioxide, causing a change in pH of the blood bathing the cerebral centers, is the most logical explanation of hyperventilation tetany.[6, 7]

Constitutional and General Factors

Age and sex. Young donors are much likelier to faint than are older ones. Although 75 per cent of the cases of severe syncope occurred in donors between eighteen and thirty-eight years old, this age group comprised only 58 per cent of the total donors (Fig. 1). There was little difference between the syncope rates in men and those in women. On closer analysis, however, it becomes apparent that young women faint much oftener than any other group of donors. As shown in Figure 2, 47 per cent of the women de-

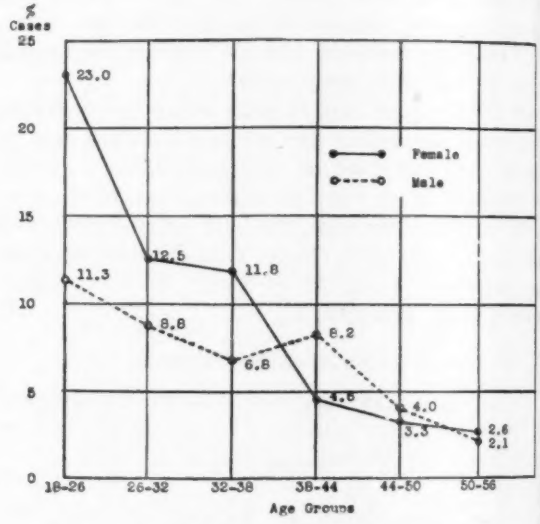

FIGURE 2. *Relation of Age and Sex to Syncope.*

veloping severe syncope were between the ages of eighteen and thirty-eight, as compared with 29 per cent of the men.

It is also interesting that in the few young women bled in the first series the syncope rate was 3 per cent, whereas in the second series, with many more young woman donors, it was 5 per cent.

Surface Area (Blood Volume) and Amount of Blood Withdrawn. It is generally believed that the amount of blood loss is an outstanding factor in the production of syncope in donors. If this is true, there should be a relation between blood volume and syncope, provided that the amount of blood withdrawn is constant. Poles and Boycott[4] found that the body surface of fainters was lower than that of non-fainters, but if it is accepted that approximately 1 square meter of body surface is equivalent to 3000 cc. of blood, the difference in both sexes between syncope and control cases in the Poles and Boycott series amounted to an average of only 0.06 square meter or 180 cc. of blood,

hardly significant figure. In the present study the surface area of donors in severe syncope differed little from that of controls; this was true of both sexes (Table 2).

In experiments with professional donors, Ebert, Stead and Gibson[9] found that if 15 to 20 per cent of the normal blood volume was removed collapse usually ensued and that this state had all the features of syncope. These authors also emphasized the role of psychic and reflex factors in collapse. In obtaining blood under the conditions outlined in this paper, however, even the donor with the smallest blood volume did not lose more than 12 per cent of his blood. Nevertheless, it seems logical to assume that a person deprived of a relatively greater percentage of blood will be less capable of adjusting the circulatory mechanism in the presence of reflex vasomotor change than those deprived of smaller amounts.

TABLE 2. *Surface Area and Blood Volume in Control Donors and Those with Severe Syncope.*

DONORS	SEX	NO. OF DONORS	AVERAGE SURFACE AREA	AVERAGE BLOOD VOLUME
			sq. m.	*cc.*
Control donors	F	114	1.66	4980
	M	78	1.91	5750
Donors with severe syncopes*	F	88	1.65	4950
	M	67	1.86	5580

*Three cases omitted because of incomplete data.

Environment. The importance of the surroundings and the attitude of the staff in the donor center has been emphasized by Williams[10] and Taylor.[1] Undoubtedly in this study the more favorable circumstances under which the first series of donors was bled contributed materially in lessening the syncope rate as compared with that in the second series.

Occupation. Fatigue, lack of sleep and dehydration due to heavy or prolonged occupations are no doubt factors in syncope.[8] Such conditions were not encountered in this study. Greenbury[3] found that young female clerical workers fainted oftener than did those in other occupations, but he did not take into account age and other factors, which appear to have much more bearing on the problem than does occupation.

TABLE 3. *Contributory Factors in Severe Syncope.*

FACTOR	PERCENTAGE	
	CONTROL DONORS	DONORS WITH SEVERE SYNCOPE
History of fainting	16	50
Nervousness	23	49
Fatigue	15	33
Fasting for over five hours	53	65
Pain from venipuncture	7	11
Donation:		
First	64	67
Second	22	11
Third or higher	14	3

Weather. It is a widespread belief that fainting occurs with special frequency in a warm atmosphere, but studies by various authors tend to discount the influence of high humidity and temperature. An investigation of these factors was carried out in this study. Although no close correlation was evident, the impression gained from clinical experience that heat and humidity contribute to higher syncope rates persists.

CONTRIBUTORY FACTORS

In addition to the constitutional and general factors, there are a number of important contributory factors in syncope. Some of these are shown in Table 3, which is a comparison of a group of 200 control donors with those in the second series who had severe syncope. An outstanding fact was the high incidence of a prior history of fainting in the syncope group as compared with that in the controls. It is also apparent that nervousness and fatigue play important roles in conditioning a person to fainting. Since fasting was common to both groups, it is difficult to evaluate. Lawrence and Plaut[11] found no significant difference in blood-sugar levels between fainters and non-fainters, and hypoglycemia probably does not enter into the picture. Pain is a relatively infrequent complaint owing to the use of local anesthesia and skillful venipuncture, and hence has not been a significant factor in syncope.

When severe syncope occurred on the first donation, the donor was not called back for further donations. Nevertheless, since nervousness and apprehension are much more evident on the first visit to the donor center than at later ones, the high incidence of severe syncope on this occasion as compared with the much less frequent occurrence on subsequent donations is understandable.

Epidemic Fainting.[12] This phenomenon was encountered not infrequently in young donors. These persons, usually from the same office or service group, would "talk each other into a faint." Promptly placing the donor in a supine position almost always resulted in a mild type of syncope, the *forme fruste* of Weiss.[12] Epidemic fainting is excellent evidence of the strong psychologic effect of suggestion.

Postural Factors. As pointed out by Weiss,[12] syncope usually occurs in the upright position. Nevertheless, in these blood donors severe syncope frequently developed in the supine position. This finding must be qualified by the fact that some delayed faintings were not reported, especially if the donor had left the center. Second, in a number of patients with mild or incipient syncope this would have undoubtedly become severe if they had been allowed to get up before the circulatory system had become adjusted. It is evident that a change in posture may bring about increased cerebral ischemia and act as a contributory factor to precipitate syncope.

DISCUSSION

The clinical features of syncope as observed in this study were quite similar to those described by

Lewis[13] and Weiss[12, 14] and to those observed more recently in blood donors by several British writers.[4, 8]

It is evident that certain constitutional and contributory factors influence the production of syncope in blood donors. The young donors, especially women, were those most prone to fainting, and as suggested by Williams,[10] this may be due to an increased vasomotor instability in younger persons. It has been pointed out that in blood donors syncope differs from the usual form of fainting in that it frequently occurs with the donor in the supine position and usually develops following withdrawal of 500 cc. of blood. Nevertheless, in this series syncope occurred without loss of blood and with the donor lying down, the attack simulating in every detail that occurring after withdrawal of blood. It seems obvious that although blood loss and posture may be important conditioning factors, they are not the *sine qua non* of syncope.

The physiologic mechanism of syncope is obscure, but its various and puzzling manifestations undoubtedly occur as a result of a number of reflex stimuli passing along both sympathetic and parasympathetic pathways. Recent studies by McMichael[15] indicate that in vasovagal collapse the fall in peripheral resistance is due to reflex dilatation of the arterioles in the skeletal muscles. It is evident that the work of McDowell[2] and other British investigators[16] will go far toward dispelling the obscurity surrounding the vasomotor and cardiovascular phenomena associated with syncope.

Treatment

Syncope may give rise to alarming symptoms, and in sever cases the patient may assume a deathlike appearance. Indeed, in some cases it is impossible to detect a radial pulse or to obtain the blood pressure for several minutes. There is no doubt that such a severe vasomotor collapse could precipitate serious trouble in subjects with latent or potential organic cardiovascular disease. For this reason the elimination of those subject to fainting is an important consideration. In common with recent British opinion,[17] it is believed that donors with a history of prior fainting should be rejected as candidates for blood donation. The high incidence of a history of easy fainting — 50 per cent of the cases of severe syncope in this investigation — has been noted by others.[10, 17] The use of donors who are excessively tired or nervous should also be avoided, and psychic factors should be eliminated in so far as possible.

For the immediate treatment of fainting the most effective measure is to place the patient in a supine position with the lower extremities elevated. It is important to keep him at rest until the blood pressure has returned to normal levels to prevent recollapse, which sometimes occurs after the donor has left the center, with subsequent fall and injury. The use of vasoconstrictor drugs such as N-methyl amphetamine, as noted by McMichael,[15] may well be employed in severe cases of syncope.

Summary and Conclusions

In an experience with 16,133 blood donors, 689 cases of syncope were encountered, an incidence of 4.2 per cent.

Detailed observations on the symptoms and signs of severe syncope are recorded. Although these were often dramatic, in no case in this series were there any serious sequelae.

The frequent history of prior fainting in a series of cases of severe syncope is especially noteworthy, and the importance of psychogenic factors in syncope is emphasized.

Recent studies give promise of furnishing new insight into the complex physiologic mechanism involved in syncope, but there is much that remains obscure. The following statement of Gowers, quoted by Weiss,[12] seems as true today as it was in 1907: "Familiar as fainting is, adequately as we seem to know it, there is much in it that we do not know. Our knowledge is enough to obscure our ignorance."

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ELECTROENCEPHALOGRAPHIC STUDIES IN DIABETES MELLITUS*

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ELECTROENCEPHALOGRAPHIC studies have become an almost routine procedure at the New England Deaconess Hospital in examining diabetic patients who have frequent insulin reactions or seizures in which hypoglycemia is considered a possible precipitating factor. Although the incidence of epilepsy among diabetic patients has not proved to be greater than that in unselected persons of corresponding age groups, the occurrence of repeated insulin reactions in a specific case always raises the question whether they are due to an abnormally rapid change in the blood sugar or to instability of the nervous mechanism — that is, to an epileptoid tendency. The electroencephalogram was therefore invoked as an aid in studying the cortical activity of patients with diabetes mellitus to establish or rule out the existence of epilepsy.

It is known that diabetic patients are more sensitive to hypoglycemia than are persons with a normal carbohydrate metabolism — a fact that Root et al.[1] have recently demonstrated in their studies of radioactive insulin and its absorption. They examined normal controls and diabetic patients given identical doses — 25 units of crystalline insulin — and found that all the latter patients developed hypoglycemic reactions, as compared to only 1 of the controls.

In experiments on normal persons the brain waves are progressively slowed by a reduction of the blood-sugar level to below 50 to 60 mg. per 100 cc., and this slowing is readily correlated with outward clinical manifestations.[2, 3] The reduction of blood sugar in normal persons by means of insulin given for short periods of time produces no irreversible effects in the electroencephalogram. Injection of sugar restores the brain-wave frequency along a smooth curve.

It is not known whether repeated insulin reactions or hypoglycemic spells can eventually produce abnormal cerebral electrical activity. It will be shown, however, that in diabetic patients subject to repeated severe insulin reactions a startling degree of electroencephalographic abnormality exists. This may be due to inherent instability of the nervous system, to repeated deprivation of essential brain foodstuffs during hypoglycemia or to recurrent cerebral edema and minute petechial hemorrhages sustained during periods of profound hypoglycemia.

Himwich[4] has shown that profound hypoglycemia may depress the brain metabolism to one quarter of its normal rate. He mentions that a late and prolonged stage of hypoglycemia may produce permanent brain damage. Gellhorn and Kessler,[5] studying insulin-sensitive rats, found that insulin hypoglycemia produced the same type of effect on the electroencephalogram as that seen with anoxia.

Concerning nondiabetic epileptic patients, the evidence as presented by Gibbs et al.[6] is that a low blood-sugar level may increase the electrical abnormality in patients with petit mal, but does not do so in patients with grand mal or psychomotor epilepsy.

TECHNIC

A Grass six-channel electroencephalogram with undistorted recording up to 50 cycles a second was used. Electrodes were applied to the frontal, parietal and occipital areas. Recordings were done in a darkened room with the patient's eyes closed. In all control subjects the blood-sugar level was determined shortly before the test. A two-minute period of overbreathing was included in every test. The records were classified as normal, borderline and abnormal, on the basis of experience with several thousand patients with and without neuropsychiatric disturbances.

RESULTS

Patients with Uncomplicated Diabetes

A group of 40 patients with uncomplicated diabetes served as controls for 35 diabetic patients with repeated severe insulin reactions. The ages of the controls ranged from eighteen to forty-nine years with an average of thirty-four years. In this range one can expect the least number of variations in brain activity caused by immaturity or by senile changes. The previous duration of diabetes was one week to twenty-one years, and 20 patients had had the disease for ten years or more. The blood-sugar levels before the electroencephalographic examination ranged from 116 to 428 mg. per 100 cc. All the patients were ambulatory and in good health. None of them had a history of seizures, personality change or neurologic disturbance. All patients but 1 were taking insulin, in doses ranging from 10 units of protamine-zinc insulin to 26 units of crystalline insulin and 76 units of protamine-zinc insulin.

The records were classified as within normal limits in 32 cases, as borderline in 5, and as distinctly abnormal in 3. Analysis of these three groups revealed no significant differences in age, sex, duration of diabetes, duration of insulin intake or type of in-

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sulin used. The following is a brief summary of the controls with definitely abnormal electroencephalograms:

CASE 1 (No. 22895). A 47-year-old woman had been taking insulin since the onset of diabetes in 1929. The dosage at the time of the electroencephalographic study was 4 units of crystalline insulin and 26 units of protamine-zinc insulin. On the maximum dose of 8 and 36 units, respectively, there were several mild reactions, with blood-sugar levels of 44 and 46 mg. per 100 cc., but no convulsions or unconsciousness.

CASE 2 (No. 13831). A 47-year-old woman had had diabetes for 9 years. Insulin had been given since 1935. At the time of the electroencephalogram she was receiving 28 units of crystalline insulin and 58 units of protamine-zinc insulin, which was the maximum dose. She had a basal metabolic rate of +30 per cent, with toxic adenoma of the thyroid gland, which was later removed. The electroencephalographic abnormality may have been related to the cerebral electrical disturbance of hyperthyroidism.

CASE 3 (No. 7336). A 43-year-old man, with diabetes of 15 years' duration, had taken insulin for the entire period, the dosage being 4 units of crystalline insulin and 20 units of protamine-zinc insulin. The blood-sugar level at the time of the examination was 428 mg. per 100 cc. There had been a recent severe insulin reaction, with unconsciousness but no convulsions. Insufficient insulin was taken by the patient because of fear of recurrence. At a subsequent office visit he was ambulatory, with a blood-sugar level of 44 mg.

These 3 patients comprise 8 per cent of the entire control group studied, which compares favorably with the incidence of cerebral dysrhythmia of 8 to 10 per cent in general unselected groups of non-diabetic persons. Lennox[7] states, "It is important to realize that even though certain individuals, probably about 10 per cent of the population, have a cerebral dysrhythmia and, therefore, presumably carry a predisposition to seizure or allied conditions, such seizures or conditions may never eventuate unless one or more of the other causes of seizure are present."

In essentially uncomplicated diabetes of long duration, the figures for electroencephalographic abnormality are quite similar to those in uncomplicated diabetes of short duration. Of the 20 patients with a long duration, — ten or more years, — 2 had abnormal electroencephalograms. In 10 patients, the onset of diabetes had occurred before the age of fifteen years. No one of these cases was recorded in the abnormal class, 2 were in the borderline group, and the other 8 were normal. This may be of interest because of the increased incidence of epilepsy in diabetic children, in whom it is 1.07 per cent, as compared with 0.84 per cent in normal children.[8] All classified as child diabetic patients have relatively severe diabetes and have taken insulin for a minimum of approximately fifteen years.

Diabetic Patients with Repeated Severe Insulin Reactions

Thirty-five diabetic patients with repeated severe insulin reactions — problem cases — were also evaluated from the electroencephalographic point of view. The clinical manifestations of these attacks included dizziness, weak spells, transient disturbances of memory, aphasia or paresis, temper tantrums, attacks of petit mal, convulsive attacks and spells of unconsciousness. In some cases hypoglycemia was known to be present and improvement occurred with the administration of carbohydrate. All patients were studied between attacks, when they had no clinical symptoms of hypoglycemia.

The ages varied from fourteen to fifty-four years with an average of 25.7 years. The duration of diabetes ranged from 5 months to twenty years, with an average of 8.2 years. Blood-sugar levels were not ascertained in all cases before the electroencephalographic tracings, but no patient had clinical symptoms of hypoglycemia at the time they were made. All the patients were taking insulin in doses ranging from 8 crystalline and 16 protamine-zinc units to 36 crystalline and 78 protamine-zinc insulin units.

The tracings were classified as normal in 8 cases, as borderline in 9, and as definitely abnormal in 18. There was no significant difference between these three groups in age, duration of diabetes, duration of insulin intake or type of insulin taken. The types of insulin reaction in all groups were quite varied.

DISCUSSION

Diabetic patients in general do not suffer from epileptic phenomena more than do members of a normal group. Similarly, electroencephalograms in cases of uncomplicated diabetes are essentially

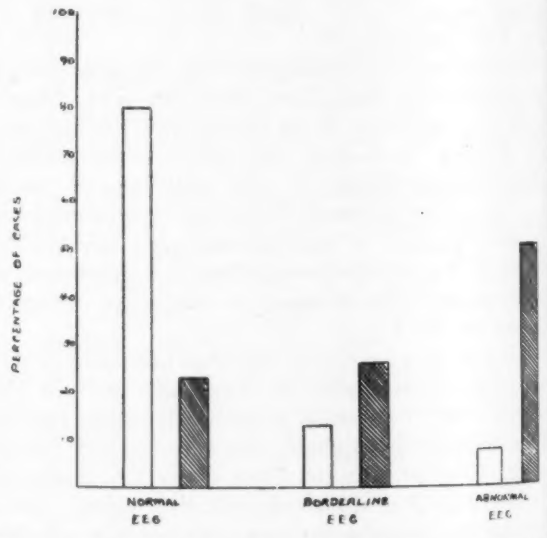

FIGURE 1. *Percentage of Normal, Borderline and Abnormal Electroencephalograms in 40 Control Diabetic Patients and in 35 "Problem" Diabetic Patients.*

The blank blocks represent the control group, and the cross-hatched blocks the "problem" group.

within normal limits. This is true irrespective of the duration of diabetes, the duration of insulin treatment or the amount of insulin administered. In clinics in which large groups of diabetic patients are studied, however, a small but nevertheless sig-

nificant fraction of cases present extreme difficulty in control by routine methods, and require special attention. These patients are inordinately sensitive to relatively minor changes in the blood-sugar level, and their clinical reactions are disproportionately severe. The manifestations of insulin sensitivity are highly variable.

In cases of this kind it is of both theoretical and practical importance to know what role the nervous mechanism plays in the fundamental instability. Because the changes primarily involve carbohydrates, the chief foodstuff of the brain, one is naturally inclined to suspect disordered function within the central nervous system. From the clinical point of view, many of the reactions involve abnormal but co-ordinated motor manifestations or specifically suggest epilepsy. Other reaction patterns, such as unconsciousness, point incontrovertibly to abnormal cerebral function.

The electroencephalographic evidence supports the theory that severe repeated insulin reactions are due not only to unstable carbohydrate regulation but also to unstable cerebral, and specifically cortical, function as well. Some of the electroencephalograms obtained were indistinguishable from interval patterns in patients suffering from grand-mal epilepsy. The incidence of abnormal or atypical brain wave tracings in the unstable group of diabetic patients is too high to be due merely to chance.

The observations established the fact that the central nervous system plays a leading role in the instability of patients with so-called "problem diabetes" or diabetes regulated with great difficulty. In this group the possibility of cortical instability should never be neglected in evaluating the functional difficulties of the patient, and by implication, proper treatment should encompass proper management of the central-nervous-system disorder. The electroencephalogram may be invoked as a valuable aid in studying diabetic patients with frequent severe insulin reactions.

Summary

In a study of 40 patients with uncomplicated diabetes, the incidence of cerebral dysrhythmia as evidenced by abnormal electroencephalograms is not increased over that in normal persons.

Long duration of diabetes does not alter the incidence of cerebral dysrhythmia.

Administration of insulin over long periods of time has no apparent effect on the electroencephalograms.

Fifty-one per cent of diabetic patients with frequent severe insulin reactions were found to have abnormal electroencephalograms.

The electroencephalograms are of aid in the evaluation of the stability of cortical function in diabetic patients with such reactions.

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SYMPOSIUM ON MEDICAL SOCIOLOGY

MEDICAL ECONOMICS*

NATHAN SINAI, D.P.H.†

THE title of this lecture is actually the inclusive title of the entire series. The series can serve only to provide a superficial view of the issues involved. If out of this view there emerges a continuing and critical analysis, the series will have had high value. If, on the other hand, the series ends with final decisions on the part of the audience, it must be concluded either that these decisions were brought to the meetings or that the speakers were highly persuasive.

In arriving at conclusions, there is an acute need throughout the country for the tested device that is such a common procedure in medicine — the device embraced in the words "examination, diagnosis, treatment." The fallacy of centering attention on treatment without any agreement concerning diagnosis, which, in turn, is based on a critical examination, is obvious. It is so obvious that one wonders at its prevalence. Because of this prevalence, about two thirds of the courses in this field for sophomore and senior medical students at the University of Michigan are purposely devoted to "examination and diagnosis."

There is one aspect of medical economics to which attention has been pitiably inadequate. Most of the discussions in the country have revolved around broad principles, broad philosophies, broad plans and broad legislation. Their very breadth excites passionate debate, but ultimately, whatever principles, philosophies, plans or legislation are adopted, these must be transformed into the realities and details of administration. So far, this fact has almost entirely escaped attention. Because of this, and in spite of the discussion, the average physician is unable to see himself and his concept of practice within the framework of any scheme that may be proposed. What are needed are fewer panoramas and many more "closeups." Some of the problems and situations that administrators must face within the framework of various broad proposals are the following.

The statement is generally accepted that the public wants and needs medical protection against so-called "catastrophic illness," but there is a tendency to leap from this to the conclusion that practically all medicoeconomic catastrophes involve the hospital and either the surgeon or the obstetrician. It is said that 10 per cent of the people pay 41 per cent of the total medical bill, the hospital, the surgeon and the obstetrician being the chief payees. But a few other facts and diagrams insist on obtruding themselves, and the word "catastrophe" then becomes less easy to define in terms of absolute costs. Indeed, it becomes a relative matter closely linked to the income groups in the country.

It will be recalled that the Wagner–Murray-Dingell Bill proposes to exclude the services of dentists. The decision to exclude them was probably based on the knowledge of the overwhelming number of existing dental defects and the lack of enough dentists to cope with the problem as a whole. Practically all those who questioned the exclusion thought in terms of at least a partial attack on the problems, especially with respect to the needs of children, but from the administrative standpoint, the exclusion raised an entirely different question.

In many parts of the country a large portion of the oral surgery is performed by specialists whose training and professional degrees are in dentistry. They are the ones who provide services in such cases as jaw fractures. If the exclusion of dentists had been adopted, the bill would have created an anomalous situation in which the services would have been included, but the many specialists who provide them would have been excluded. It is not intended to imply that this was the intention of the authors of the bill; the statement is only one of what would have happened in its administration.

To the administrator, the role of medical care as a buttress for other systems of security is a weighty one. It is estimated that by the end of the next thirty years persons above the age of sixty will comprise almost a fifth of the population. Only a cursory examination of the curve of illness according to age is necessary to reach the conclusion that old-age annuities cannot provide protection against the concentration of illness in the upper age groups. The same general conclusion is warranted as concerns unemployment payments under a system of unemployment insurance.

On the subject of security, another movement taking place in the country deserves much more attention. It is the movement toward disability compensation. There is danger in reasoning by exact analogy, but the only greater danger lies in discarding all previous experience. Workmen's compensation legislation swept the country be-

*This is the fourth of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March, 1945; they were sponsored by the Department of Preventive Medicine and were primarily intended for third-year students. These articles will temporarily replace the reports "Medical Progress."

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tween 1910 and 1915. There is now the pressure behind disability compensation. The original concept of workmen's compensation was one of weekly cash payments during the period of disability. This concept is held with respect to disability compensation. Soon after the initiation of workmen's compensation, the fact that people were not using their weekly payments to purchase necessary medical care became evident. It also became evident that the provision of medical care would "pay dividends." Hence, medical services were introduced as a part of workmen's compensation; the services have steadily increased, and today any proposal to exclude such services would be regarded as contrary to sound policy. The parallel presents itself in disability compensation. It will be interesting to see how long such a system as that in Rhode Island operates without medical services as a part of the scheme.

There are many questions that involve the combination of independent group practice and group payment. Here, too, the administrator thinks in terms of practical application. The qualitative values of group practice are seldom questioned, but within the group, recognition must be given to certain essentials: the income for each member must be reasonably adequate, and his tenure as a member of the group must be reasonably stable. Assuming that a group is organized to serve 50,000 people on a voluntary prepayment basis, the population must be one whose income is stable. Thus, it cannot be one of 50,000 today and one of 30,000 a year later owing to umemployment. A medical group dependent for its stability on a continuing income and having a staff large enough to care for 50,000 people might weather a short-term decrease to 30,000, but it could not weather a long-term one. It is for this reason that the most successful medical group practice under a system of voluntary prepayment is the one that includes that small portion of the population with stable incomes — policemen, firemen, schoolteachers and others with annual salaries. To include industrial populations with extremely fluctuating levels of employment means that the medical group must face the difficult problem of preparing against abrupt decreases in income. If this preparation is inadequate or impossible and the emergency comes, the group is threatened with disintegration.

Mention has been made of voluntary prepayment. The question of compulsion *versus* volition is presented as one of the sharpest issues of the day. But it is not really so sharp as it has been drawn. There are many forms of compulsion other than legal. There is the pressure of sales, the pressure of group or public opinion, the moral pressure of employers on employees and the even greater pressure exerted by employer contributions as partial payment. Actually, the issue is becoming less and less one of compulsion *versus* volition and more and more one of legal compulsion *versus* quasi-compulsion.

There is another broad generalization that calls for much more critical examination. It has to do with the method of compensation for services; from the administrative standpoint it causes apprehension. The evidence is fairly clear that, whatever the future prepayment plan for medical care, it will begin with fees for specified services as the method of compensation to physicians. There may be changes to so-called "capitation fees" or ultimately to salaried services, but the administrator must deal with immediate problems, not with ultimate possibilities.

The fee-for-service method of payment has a long and broad history of failure. It is unlikely that it will work merely because of resolutions that describe it in flattering terms and declare it to be "the American way." Not only did it fail yesterday but it is failing today. Even though an appendectomy rate of 25 per 1000 subscribers, for example, does not endanger the economic foundation of a prepayment plan, such a rate is approximately triple the normal one and points to a need for administrative action; absence of action means another failure for the system. "Control" is a hated word, but the application of necessary and fair control measures is not nearly so dangerous as is the continued evasion of brutal facts. The fee-for-service method if applied with all the ingenuity of which administrations are capable might be made to work; applied without such ingenuity it has in it the elements of a national calamity.

The final example of administrative problems in prepayment programs relates to the two major forms of the benefits to subscribers. In one case the subscriber's contract calls for services; in the other, the benefits are distributed in cash. In the first case, the subscriber would receive an appendectomy and the surgeon would be compensated directly from the fund, probably receiving $100 as full payment for the service. In the second case, when the subscriber presents written evidence than an appendectomy has been performed, the company or the plan indemnifies him, a check being sent either to him or directly to the surgeon.

All this appears to be six of one and half a dozen of the other. Whereas the great majority of the voluntary plans provide services, the insurance company plans indemnify in cash. It is the recommendation of many medical societies that the principle of cash indemnity be applied; yet if the principle is widely applied, it is doubtful that it can withstand the accumulative weight of public disfavor.

As an insurance device, cash indemnity as now used is unsound. The subscriber purchases in good faith what he interprets as protection, but not until the contingency arises is he able to learn the degree of his protection. It may be 100 per cent or 50 per cent, depending on the charge for the service. No other form of insurance could exist if this principle

were used — if the protection purchased remained a mystery to the purchaser until he needed protection.

From the public viewpoint, and considered in terms of reality, certain responses to the situation in some existing plans are disturbing. When a patient who carries hospital-service insurance but has cash-indemnity medical protection inquires what a surgical fee will be, he may be asked whether he carries hospital insurance and surgical insurance, and if he replies in the affirmative the surgeon may say: "That's very fortunate. It is a fine thing to have such protection. My fee will be $200." The question about insurance may not be so abrupt or so pointed, but however it is put, the patient is aware that he has answered it. Too often a by-product of the experience, whether or not it is justified, is an unanswered question in the mind of the patient and concerning whether the fee was much larger as a result of the protection than it would have been without such protection. This question does not leave the physician in an enviable position. Its end result, a loss of public confidence, is predictable in terms of public antagonism.

Enough has been said to indicate a primary need for practical methods in medical economics. Without far more attention to administrative methods and details and to the organization of administrative experience, no plan can proceed from broad principles to satisfactory applications. It is administrative method that will influence and finally determine the medical, social and economic soundness of any plan.

Over the country there is abundant administrative experience, but it is a misfortune that so little of it has been accumulated. Except for experience with hospitalization plans in connection with Blue Cross organizations, there has been little centralization of experience. It is for this reason that in our own work at the University of Michigan we have emphasized administration and administrative technics.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32041

PRESENTATION OF CASE

A twenty-nine-year-old clerk entered the hospital complaining of recurrent pain in the flanks.

Eight years before admission he had an attack of sharp pain in the right flank, and later passed several stones by urethra, followed by slight bleeding, which lasted for thirty hours. Another stone was passed two years later, and on chemical analysis was found to consist of calcium phosphate. A third attack of pain in the right flank and passage of stones occurred three years before admission, while in the Army. Similar episodes recurred four and eight months later. The sixth passage of stones took place eight months before admission; at that time another stone was detected by x-ray examination in the right renal pelvis and a right nephrolithotomy was performed. Several weeks later, pain was noticed in the left flank for the first time and stones were again passed. The patient was later discharged from the Army.

Weakness and fatigue had not been marked. For three years, however, the patient had not been able to resume the upright position after leaning over. No polyuria, frequency or evidence of renal infection had been noted. The appetite had been good, and he had complained of no bone pain. Four years before admission he had sustained a traumatic fracture of the left fifth metacarpal; healing was normal. The teeth had been in good condition. His maximum weight had been 140 pounds, three years before admission; at the time of admission his weight was 120 pounds, with no recent loss.

Physical examination revealed a thin, pale man in no discomfort. The pharynx was moderately injected, with a postnasal drip. The teeth were normal. The trachea was slightly deviated to the left, with a questionable soft-tissue fullness on the left. The heart was not enlarged. A soft systolic murmur was heard over the apex. The lungs were clear. There was no costovertebral-angle tenderness. The bones were normal. Neurologic examination was negative.

The temperature was 99.2°F., the pulse 80, and the respirations 20. The blood pressure was 130 systolic, 75 diastolic.

The hemoglobin was 14.7 gm. The urine contained an occasional white cell, mucin and calcium oxalate crystals. A twenty-four-hour urine specimen, which had a volume of 1688 cc., contained a total of 288 mg. of calcium. The serum calcium was 10.7 mg. per 100 cc., the phosphorus 3.0 mg., and the alkaline phosphatase 4.0 Bodansky units. Determinations the next day were as follows: serum calcium 10.7 mg. per 100 cc., phosphorus 3.1 mg., and alkaline phosphatase 4.9 units. The total serum protein was 6.0 gm. per 100 cc. A blood Hinton test was negative.

An x-ray film of the teeth showed no paradental disease; the lamina dura was preserved but of unusual thickness. The bones of the jaw were not so dense as usual, and the trabeculae were coarse. The bones of the lumbar spine and pelvis, the upper portions of the femurs and the lower ribs showed some decalcification; the cortices were thinned, and the trabeculae coarse. No urinary calculi were evident. Several areas of increased density overlay the cecum.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ALLAN M. BUTLER: Either the clinicians who took care of this patient were extremely wise or they had more data than those given in this abstract on which to base the decision to perform an operation. We have no information about renal function. We have only the statement that no evidence of renal infection was found on one examination. There was no intravenous pyelogram, and no determination of the serum carbon dioxide and chloride. Is that correct?

DR. BENJAMIN CASTLEMAN: We have given you all the information that was in the record.

DR. BUTLER: Then I must confess that, not being so intelligent as the physicians who took care of this patient, I should have demanded that information before doing an operation.

We shall now consider the x-ray films. I wish that we had a roentgenologist to interpret them, for I see nothing suggesting why this man was unable to resume the upright position after leaning over. Do you see anything in the films, Dr. Aub, that would cause this?

DR. JOSEPH C. AUB: No.

DR. BUTLER: Of course, one thinks of arthritis and of intervertebral disk, but without a roentgenologist, I shall pass on.

DR. AUB: I think there is a little decalcification.

DR. BUTLER: Yes, but it appears minor.

DR. AUB: I am not so sure.

DR. CASTLEMAN: The x-ray report states that there was some decalcification. The cortices were thin.

DR. BUTLER: The trachea was slightly deviated to the left, with a question of fullness on the left. We have no x-ray films of the neck region. Parathyroid tumors are almost never palpable. The deviation was to the left and the fullness was on the left. I shall pass that over, because I cannot explain it.

At the end it states that several areas of increased density overlay the cecum. I am unable to interpret the significance of these spots, and I take it that the x-ray man could not interpret them.

We then come to a discussion of the etiology of the renal calculi, from which this man had suffered for eight years. First, we think of renal disease. It may be infection, particularly with an ammonia-producing organism. We merely have this single statement in the record that there was no evidence of renal infection. So our evidence regarding infection is extremely meager.

DR. FULLER ALBRIGHT: There were two negative cultures.

DR. BUTLER: That being the case, at the time of his last examination he did not have evidence of renal infection, but that, of course, does not rule it out.

The next thing to consider is renal stasis. The evidence again is meager, because we have no information about a renal-function test and an intravenous pyelogram. There is a type of renal disease associated with diminished ability of the kidneys to produce ammonia and thus to conserve base in the excretion of urine; this results in excessive loss of calcium and other cations (base) and thus in acidosis.

DR. ALBRIGHT: The serum carbon dioxide and chloride levels were normal.

DR. BUTLER: Serum chloride in patients with renal calculi is not infrequently found to be elevated, and because of that elevation, there is a diminished carbon dioxide, and a chloride acidosis, which accentuates the acidosis that comes from the loss of base just referred to above. This type of renal disease, with the chloride acidosis, loss of base and increased excretion of calcium, is usually a disease limited to the renal tubules, and in the tubules there is not infrequently a deposition of calcium phosphate. All the evidence so far is against that type of renal disease, largely because if there is an acidosis with any type of renal disease, and an excessive loss of calcium in the urine, the patient usually has an elevated alkaline phosphatase of the serum. Here the alkaline phosphatase of the serum was normal.

Then we come to cases of extensive renal disease, with renal insufficiency. This can be ruled out promptly with the data available, because with that type there should be an elevated nonprotein nitrogen and inorganic phosphorus, a diminished serum calcium and carbon dioxide and an elevated phosphatase, none of which were present in this case.

The second major cause of renal calculi that one ought to think of is atrophy of bone. One might think of atrophy of disuse. In this case, however, the history is not indicative of atrophy associated with disuse. Dr. Albright has recently called attention to a patient who presented a difficult differential diagnosis between hyperparathyroidism and atrophy of disuse. Dr. Howard,[1] of Baltimore, has called attention to a patient who, following a fracture, was given a large amount of vitamin D and developed hypercalcemia, anuria and uremia. We have had a fairly extensive series of cases of so-called "resistant" rickets and have found that, following corrective osteotomies, there is often a marked elevation in the serum calcium and inorganic phosphorus, a fall in the alkaline phosphatase to normal and complete healing of the rickets, which for years had been resistant to treatment with huge daily doses of vitamin D.

Another cause of bone atrophy may be Cushing's syndrome. There is, however, no history suggestive of a Cushing syndrome. Of course, if the demineralization of the bones as shown by x-ray were due to steatorrhea, there would not be increased calcium in the urine and calculi.

Finally, we come to hyperparathyroidism. Dr. Albright and his colleagues have described a disease that can occur with minimal bone disease, but in most of the cases that they have reported there has been some elevation of the serum calcium. Because of the long-standing condition in this patient, however, and the demineralization and depletion of calcium, hyperparathyroidism may have been present without elevation of the serum calcium. Their cases showed a minimal change in the inorganic phosphorus and no elevation of the phosphatase. This patient's inorganic phosphorus was just at the lower limit of normal. The calcium of 10.7 mg. for a serum protein of 6 gm. is just above the upper limit of normal, by the accurate method used here.

In the absence of evidence pointing to renal infection and in the absence of such lowered carbon dioxide and of elevated phosphatase as would be consistent with a renal condition that would result in this much decalcification of bone and this degree of increased excretion of calcium, my diagnosis is either a small parathyroid adenoma or a so-called "idiopathic hypertrophy" of the parathyroid glands.

DR. CASTLEMAN: Hypertrophy of all four glands?

DR. BUTLER: The idiopathic hypertrophy that involves all four glands, the enlargement being due to an enlargement of the cells rather than to a great increase in the number of cells, such as one sees in secondary parathyroid hyperplasia following renal disease.

DR. CASTLEMAN: Dr. Reifenstein, would you like to comment?

DR. EDWARD C. REIFENSTEIN: There is not much that I can add to the discussion, except to say that we never did obtain an adequate medical history

This man had been in the armed forces and at time of discharge was referred to this hospital. We tried to get the medical history from the Army. He reported that he had been sent in with a question of hyperparathyroidism because the blood chemical findings while he was in the Army had been quite abnormal. (The phosphorus values were reported to be between 2.9 and 4 mg., and the calcium as high as 14 mg. per 100 cc.) The medical officer considered a diagnosis of hyperparathyroidism and suggested to the patient on discharge that he come here for further study. Our records include some additional data. The patient had a negative urinary culture, and although we examined the urinary sediment quite carefully, we could find no evidence of urinary infection. We, too, ruled out a renal condition as a cause for the abnormal blood chemical findings.

DR. ALBRIGHT: Why did Dr. Butler think of parathyroid hypertrophy?

DR. BUTLER: Because of your work, Dr. Albright.

DR. ALBRIGHT: The disease is extremely rare.

DR. BUTLER: You reported an excellent series of cases in the *Archives of Internal Medicine*.[2]

DR. OLIVER COPE: I might say that the patient was here during the peak of the shortage of x-ray films, which explains some of the lack of films. The X-Ray Department only had a day or two's supply of film on hand and asked us to cut down on any unnecessary examinations. We were a little confused because the original serum calcium determinations in the Army were 14 and 12 mg., and it looked as if these values were accurate. Our values were lower than anticipated. Three determinations were below 11 mg. per 100 cc., and we have accepted this as the minimum to make a diagnosis of hyperparathyroidism. That discrepancy, of course, contributed to the confusion and is emphasized because so much stress has been placed on the level of the serum calcium.

We thought that this patient had hyperparathyroidism, and I explored the right side of the neck first on a 50-50 chance. I could not find an enlarged parathyroid gland on the right side, so I went to the left and, after exposing the posterolateral surface of the thyroid gland, I saw some vessels that should not have been there. They were a little large, and they went down behind the thyroid gland and the esophagus. I found what appeared to be a small adenoma in the upper gland. It was round and light in color — in parathyroid hypertrophy the glands are irregular in shape and a little more chocolate in color than an adenoma. I then found quite easily a lower parathyroid gland on the left, which appeared to be normal in size and to have the correct color.

CLINICAL DIAGNOSIS

Parathyroid adenoma.

DR. BUTLER'S DIAGNOSIS

Hyperparathyroidism due to either a small adenoma or idiopathic hypertrophy.

ANATOMICAL DIAGNOSIS

Parathyroid adenoma.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This was a small adenoma, measuring about 8 by 6 by 4 mm. A normal gland measures 6 by 4 by 2 mm. There was a rim of normal parathyroid tissue around a part of the adenoma, which is what one should always look for in making a section of an adenoma. The presence of this rim of normal gland is evidence in favor of neoplasm and rules out hyperplasia. Hyperplasia involves the entire gland and does not leave a rim of perfectly normal tissue.

DR. REIFENSTEIN: The blood chemical findings after operation are of interest. On the following day, the calcium was 8.7 mg., and the phosphorus 2.6 mg. per 100 cc. Three days after operation the phosphorus was 3.8 mg., and the alkaline phosphatase 3.0 Bodansky units, and on the fourth day the calcium was 8.0 mg., the phosphorus 3.7 mg., and the phosphatase 1.9 units. The Sulkowitch test for calcium in the urine was ++++ before operation, +++ two days after operation, and + to zero thereafter.

DR. CASTLEMAN: Do you think that we should consider a serum calcium of 10.7 mg. as being above normal?

DR. BUTLER: The upper limit of normal, with a normal serum protein, is about 10.5 mg. This patient's serum protein, however, was down to 6 gm. per cent.

DR. ALBRIGHT: Our average normal runs about 9.5 mg. per 100 cc.

DR. BUTLER: The serum protein concentration of most hospitalized patients is down a little, and that means the serum calcium concentration is correspondingly lowered.

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CASE 32042

PRESENTATION OF CASE

A seventeen-year-old schoolgirl entered the hospital complaining of pain in the right pubic region.

Six months before admission she first noticed a "nagging" pain in this area. It grew steadily severer and came to involve the right hip and thigh down to the knee. She walked with a limp and with increasing difficulty. She had lost about 10 pounds

in weight during her illness and had become definitely weak and anorexic.

The past history was negative except that one year before admission the patient had bruised her right hip in an accident. Two years before admission, she had had an attack of "arthritis" in the knees.

Physical examination revealed a somewhat undernourished, sallow girl in no acute distress. Examination of the head, neck, heart, lungs and abdomen was negative. Attached to the right pubic ramus near the midline was a tender hard mass. There was tenderness also over the anterior aspect of the right femur and knee.

The temperature was 99°F., the pulse 100, and the respirations 25. The blood pressure was 120 systolic, 80 diastolic.

The hemoglobin was 12.2 gm. The white-cell count was 10,400, with 59 per cent neutrophils. The red cells and platelets appeared normal in a stained smear. The serum calcium was 9.6 mg. per 100 cc., the phosphorus 2.4 mg., and the alkaline phosphatase 3.2 Bodansky units. The urine was normal.

An x-ray film of the pelvis revealed a destructive lesion involving the right superior ramus of the pubis and extending from the symphysis well toward the acetabulum (Fig. 1). There was some periosteal reaction about it, and apparently a soft-tissue tumor into which radiating spicules extended. No other bony lesions were found. The lungs were clear.

An operation was performed.

FIGURE 1. *Roentgenogram of Pelvis.*

DIFFERENTIAL DIAGNOSIS

DR. IRA T. NATHANSON: May we see the x-ray films?

DR. MILFORD D. SCHULZ: These films show an area of destruction involving the right pubic bone. A soft-tissue mass can be seen about it, into which spicules of bone extend. There is so-called "layering" where the periosteum has been lifted, and there seems to be a lot of disorganization of the normal medullary pattern. No remote disease is evident.

DR. NATHANSON: An essential point to be considered in the diagnosis is whether the lesion is inflammatory or neoplastic. I shall discuss inflammatory lesions first.

Osteomyelitis is one of the most frequent of the inflammatory lesions. In favor of this diagnosis are the age of the patient, the pain and the progressive character of the process. Against it are the x-ray evidence of destruction of the periosteum, as suggested by a soft-tissue tumor, and the lack of the sequestration and new-bone formation usually seen in an osteomyelitis of relatively long duration. In osteomyelitis the periosteum is elevated but seldom penetrated. The site of the lesion is also unusual for such a disease. The white-cell count may be elevated but not necessarily so, particularly in the chronic phase of the disease. Loss of weight and generalized debility are uncommon except in the late stages.

Tuberculosis is extremely rare in the pubis, and as a rule, tuberculous lesions of this character are

not seen without other manifestations of the disease. In addition, this disease usually arises in the neighborhood of the joint and involves the capsule and cartilage.

Syphilis can be eliminated on the basis of the site, the character of the lesion, the age of the patient and, particularly, the absence of other evidence.

Other lesions in which the etiology is less definite must also be considered. Eosinophilic granuloma is frequently seen in young people, may occur anywhere, but generally in flat bones, and may give symptoms of pain and evidence of tumor. X-ray examination usually reveals a destructive lesion. It is seldom debilitating, however, and rarely gives rise to such symptoms as described in this patient. Osteoid osteoma usually presents as a small lesion and causes few symptoms. On x-ray examination it stands out from the surrounding osseous tissue as a delimited nidus, and there is evidence of calcified atypical new bone.

What are the possibilities of neoplastic disease? The history, symptoms and physical findings strongly suggest a neoplastic process. Osteochondroma, a benign lesion, may appear in the pubis, but it can be eliminated by the x-ray evidence itself. Of the malignant lesions, there are a number of possibilities. Malignant lymphoma involving bone, particularly the reticulum-cell sarcoma type, may primarily arise in a single bone and remain confined in that location for a considerable time. It usually, however, is slowly growing and is rare in the pubis, and there are seldom constitutional symptoms, even when the tumor becomes large. Although it may exhibit evidence of bone destruction by x-ray, a soft-tissue mass is rare, except in certain locations.

Osteogenic sarcoma generally arises in the metaphyses of long bones, although one type especially, the chondrosarcoma, may arise in the pubis. Even the latter is unusual in this location. These tumors are usually prevented by the periosteum from breaking through and invading the soft tissue for a considerable period. When the soft tissues are invaded there may be evidence of calcification. In this patient there was no elevation of the alkaline phosphatase, but this does not eliminate an osteogenic tumor, particularly one of the osteolytic type. The x-ray films are not characteristic of an osteogenic sarcoma, although there is periosteal reaction, which in itself is insufficient to make a diagnosis. Pain is frequently an early symptom, but except in the late stages of the disease, disability is usually absent and the general status of the patient is surprisingly good and out of proportion to the extent of disease and the degree of malignancy.

Myeloma usually occurs in persons over forty and is generally present in multiple sites when the patient is first seen.

Metastatic lesions from primary tumors elsewhere are unusual in this age group and seldom give rise to soft-tissue tumors.

The one tumor that fits the clinical syndrome is Ewing's sarcoma. It is a tumor of growing bone and arises from the bone marrow. The long bones are usually affected, but flat bones, particularly those of the pelvis, are not infrequently involved. The disease causes bone destruction as it develops, and by x-ray the bone has a moth-eaten look. The periosteum becomes reactive and lays down new bone, often in layers, leading to the characteristic onion-skin appearance. Sometimes radiating spicules may be seen, thus causing confusion with osteogenic sarcoma. The disease may penetrate the periosteum. This is especially true in flat bones, where the tumor breaks through the periosteum early and invades the soft tissue, such as occurred in this case. There is seldom evidence of new-bone formation in the soft-tissue mass. Pain is the most frequent initial symptom. At first it is intermittent, but as the disease proceeds it becomes increasingly severe and persistent. The tumor usually cannot be palpated until a considerable time after the onset of symptoms. It is frequently tender, firm and irregular. The overlying skin may be warm, red and edematous, which not infrequently leads to an erroneous diagnosis of osteomyelitis. Although there is no such statement in the history, the disease is often accompanied by bouts of febrile reactions, which also suggest an inflammatory process. Constitutional changes, such as weakness and loss of weight, are often seen in Ewing's sarcoma. Pain and sensory disturbances arise from growth of the tumor within the marrow cavity and eventual involvement of the sensory nerves. Depending on the location, difficulty in motion and a lump may result from soft-tissue as well as motor-nerve involvement. Laboratory evidence is of little aid in the diagnosis. Occasionally the white-cell count is abnormal, but the alkaline phosphatase is rarely elevated.

In view of the above facts the most probable diagnosis is Ewing's sarcoma.

Dr. Schulz: It might be noted that within the past two years, we have seen at least three patients with Ewing's tumor in a comparable location.

Dr. Ernest M. Daland: This patient was operated on under novocain anesthesia. A palpable lymph node overlying the ascending ramus was removed; it appeared to be merely hyperplastic. The incision was deepened down to the bone, and tumor was found. A specimen was removed with a curet. There was a gush of white fluid that at first suggested pus but then seemed more typical of the fluid often seen with Ewing's sarcoma. The wound was closed without drainage.

Clinical Diagnosis

Ewing's sarcoma of pubis?

DR. NATHANSON'S DIAGNOSIS

Ewing's sarcoma of pubis.

ANATOMICAL DIAGNOSIS

Ewing's sarcoma of pubis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The biopsy confirmed Dr. Nathanson's diagnosis of Ewing's sarcoma. The lymph node showed only hyperplasia.

DR. DALAND: The patient was treated with the million-volt machine, receiving a total of 5400 r, half anteriorly and half posteriorly, over a period of approximately three weeks. After the second treatment she had practically complete relief. After the fourth treatment she was able to move her leg quite normally and opiates were stopped. By the time the treatments were completed, she had complete relief of pain and normal hip motion.

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FEDERAL SUPPORT FOR SCIENCE IN PEACETIME

Penicillin and the atomic bomb, with their enormous but opposite potentialities for good and for evil, were brought into a world at war by scientists subsidized by the federal government. These and other achievements of integrated scientific endeavor financed by federal grants have suggested the extent of the benefits that might accrue to our society in peacetime as a result of governmentally subsidized research. Over a year ago the late President Roosevelt sought an opinion on this matter from Dr. Vannevar Bush, director of the Office of Scientific Research and Development. The reply given by Dr. Bush[1] was written after consultation with committees of experts on medical science, natural science, the discovery of scientific talent and the publication of scientific information. The report leaves no doubt in the mind of the reader concerning the immense potential advantages of a vigorous and flourishing science for improving human knowledge, economic status and health.

The need for federal support of scientific research arises primarily from the fact that the latter is expensive. Research, especially so-called "basic research," is a necessary preliminary to the applications of science, which are so obviously useful to medicine and other subjects. Basic research is carried out for the most part in universities or in nonprofit research institutes. It is often time consuming, always obscure and, because it seldom leads directly to practical results, seems to yield little tangible value relative to its cost. Applied research also is often expensive, but with practical objectives already clearly in view it is likelier to receive support from industry or other private sources than is basic science. Unfortunately, there is ample evidence that research is receiving progressively less support in the form of income from endowment, grants from foundations and private donations. Indeed, many of the seventy-seven medical schools in this country have never had sufficient funds to carry on more than a small amount of investigation. There is also a chronic deficiency of trained scientific talent, and this scarcity has been acutely increased by diversion to the battle fronts of students who otherwise would be preparing for careers in science. To restore university research even to its prewar level of scientific personnel will be a costly and prolonged educational undertaking. To accelerate scientific progress by discovering and fully utilizing the scientific talent and by developing the necessary laboratories of the country as a whole exceeds the capacity of the private sources of income that can be visualized today.

As physicians, we are impressed in our daily lives with the difficulties of appropriately applying the established findings of medical science to the individual patient. Yet, it is only necessary to consider the increasing incidence of cancer and degenerative diseases and of mental illness to understand that more hospitals and better diagnostic procedures, however useful, do not provide a solution. Better educational facilities for doctors also

will not suffice, for nowhere in the world today exists the knowledge of how to prevent or cure many of the important causes of death or chronic disability. If medicine is to continue to advance, science has to find the answers.

Granted then that the need for research is so great that federal support is required, the question of fundamental importance to scientists and the public is whether such powerful assistance can be given without impairing the independence, imagination and freedom in experimental endeavor of the individual investigator, which is so essential for scientific progress. The Bush report considers that this is possible, provided that certain basic principles remain inviolate. Thus, there must be stability of funds for long-range programs administered by an agency headed by competent and impartial citizens. The agency should promote research in organizations outside the federal government, and to these should be left, so far as possible, the choice of subject and method of investigation.

Last July the essential purposes and plan of the organization outlined by the Bush report were embodied in a bill that was introduced by Senator Magnuson, of Washington. This bill proposed the establishment of the National Research Foundation, with divisions concerned with support of research in various departments of science, including medicine, scholarships for promising science students throughout the nation and the promotion of international exchange of scientific information. A few days later a bill was introduced by Senator Kilgore, of West Virginia, proposing the establishment of the National Science Foundation, also committed to the desirable objectives just mentioned.

The differences in the organizational features of the two bills indicate why the Magnuson Bill received the enthusiastic support of most of the scientists who testified at the hearings on both bills, which were held during October before joint Senate committees. Certain government officials, however, have expressed disapproval of the plan favored by the scientists. Alarmed by the potential dangers to the future of scientific research that they foresaw might result from significant modifications of the original Magnuson Bill, a group of scientists and educators comprising the Committee Supporting the Bush Report[2] recently addressed an open letter to President Truman. In this communication the principles on which they believe that sound legislation should be based are stated and certain features of the Kilgore Bill are adversely criticized.

In the first place, the men comprising this group emphasize that the Magnuson Bill is designed to implement the plan developed by the careful studies of Dr. Bush and his advisory committees. They are in favor of the provision of the Magnuson Bill that places the direction of the foundation in the hands of a board composed of laymen and scientists appointed by the President, with a full-time administrator appointed by and responsible to the board. They express opposition to the provisions of the Kilgore Bill for the appointment by the President of a single director, together with an advisory board, because they believe that the director "should be the agent — not the master — of the board." They point to what they regard as a further defect of the Kilgore plan, namely, the provision that calls for representation on the advisory board by *ex-officio* members responsible for the scientific programs of the Army, Navy and other governmental departments. This representation, they allege, would not make for a strong and impartial advisory board

MASSACHUSETTS MEDICAL SOCIETY
POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to:

George L. Schadt, *Chairman*
Postwar Loan Fund
8 Fenway
Boston 15, Massachusetts

and would tend to promote the special interests of these governmental departments. They contend that, although knowledge of and liaison with governmental scientific activities should be maintained, the board should not be burdened with "efficiently programing and co-ordinating all federally financed research and development," as recommended by the Kilgore Bill. On the subject of the management of patients arising in the course of research supported in whole or in part by the foundation, the Magnuson Bill is silent. The members of the Committee Supporting the Bush Report regard this omission as desirable, because they believe that to specify a partial solution of this complex problem, as is attempted in the Kilgore Bill, is premature in view of the fact that a study of the Government's patent policy is now in progress by a committee headed by the Secretary of Commerce.

In his message to Congress President Truman recommended the inclusion of the social sciences within the framework of the proposed foundation. Both bills as presented to the Senate committees in amended form include the social sciences — sociology, political science, economics, law and so forth — as fields in which scientific research and development are to be supported. Although recognizing the national importance of social studies, the Committee Supporting the Bush Report expresses the view that a board fully competent to administer grants for research and fellowships in the basic sciences would not be qualified for corresponding duties with respect to the social sciences. Consequently, it is suggested that the subject of research and education in the social sciences should be taken care of in a separate body, set up, presumably, after factual study of the needs for federal support of the social sciences comparable to that which led to the framing of the Bush report.

On December 21, a third bill, sponsored by Senators Kilgore, Johnson, Pepper, Fulbright and Saltonstall was introduced. This bill retains the general objectives with respect to research and education of its predecessors, and meets some of the objections to the Kilgore Bill that have been raised by the Committee Supporting the Bush Report. Thus, *ex-officio* representation of governmental departments is not required on the advisory board, but is provided for in a separate interdepartmental committee. The administrator, who is appointed by the President remains in charge of the foundation. He is required to consult and advise with a board composed of nine persons appointed by the President but also including the chairmen of from eight to eleven divisional scientific committees appointed by himself with the approval of the board. Patents taken out in the course of research and development authorized by contracts between the foundation or any other governmental agency and a private organization are, with certain exceptions, based on the extent of the latter's contribution, to be freely dedicated to the public. A division of social sciences is retained. Expenditure of 25 per cent of the funds is placed beyond the judgment and discretion of the administrator and his committees. It is provided that this sum be distributed among the tax-supported colleges and universities, including the land-grant colleges, according to a formula based partly on state populations. The germ of this proposal appears nowhere in the Bush report.

Subsequently, another group of scientists, comprising the Committee for a National Science Foundation, released a statement outlining its views concerning the feasibility and practicability of scientific advance under governmental auspices. The six major points are as follows: the necessity for federal support of research to supplement private funds; the inclusion of provision for all fields of fundamental scientific inquiry relative to national interest; the publication of findings resulting from federally financed research and dedication of these findings to "the welfare of the people"; the training of research personnel; and the devising of a plan of organization that meets the major objections to vesting administrative responsibility in either a governing board or a single administrator.

Obviously there can be honest differences of opinion concerning the best legislative approach to the vital problem of federal support for the scientific endeavor of the Nation. In accordance with democratic procedure, the evidence for these different points of view has been presented at the Senate hearings, and it is to be hoped that Congress

will produce a satisfactory measure. Scientists do not pretend to set themselves up as authorities on administrative procedure, but their own experience justifies their right to profess knowledge of the type of organization in which they would have confidence and of the particular conditions necessary to the most fruitful efforts of the research worker. Thus, what is wanted most of all in a national research foundation is not so much co-ordination by an efficient central organization but a means for impartially discerning and aiding the all important, but remote and often obscure, peripheral human units of the plan — those men and women whose curiosity about the phenomena of nature is truly compelling. The scientists are right when they say that in such persons lie the most important scientific resources of the Nation in peace, as has been so clearly shown to be the case in war.

References

1. Bush, V. *Science — The Endless Frontier.* 184 pp. Washington, D. C.: Government Printing Office, 1945.
2. Chambers, R., and Nicholas, J. S. Pending legislation for federal aid to science. *Science* **102**:545-548, 1945.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

KNOWLTON — Edward A. Knowlton, M.D., of Holyoke, died August 22. He was in his sixty-third year.

Dr. Knowlton received his degree from Tufts College Medical School in 1909. He was senior visiting surgeon, Holyoke Hospital, visiting surgeon, Providence Hospital, and consulting surgeon to the Belchertown State School. He was former chairman of the Massachusetts Board of Registration in Medicine. He was a fellow of the American Medical Association and the American College of Surgeons.

MEDICOLEGAL ABSTRACT

Relation of Patient and Physician: Liability for malpractice. Where a plaintiff is injured by an instrumentality entirely within the defendant's control under circumstances that would not arise unless someone had been negligent the courts apply the doctrine of *res ipsa loquitur*. The plaintiff by showing such circumstances raises a sufficient inference of negligence to go to the jury and, unless the defendant comes forward with a satisfactory explanation, to obtain a verdict. Various courts have made different applications of this doctrine — some strict, some liberal.

In a recent Arkansas case the plaintiff had a needle imbedded in her foot. The defendant examined her with a fluoroscope and performed an exploratory operation. About four or five days later the plaintiff's foot became inflamed.

The plaintiff sought to found her case on *res ipsa loquitur*. The court said that the fact that unfavorable results do not ordinarily follow such a treatment does not raise an inference of malpractice by itself when unfavorable results do happen to occur. It went on to say that *res ipsa loquitur* does not apply to the practice of medicine and surgery or to the use of x-ray machines. Medicine and surgery are inexact sciences, and doctors are not guarantors of results. The implication of this last sentence is that *res ipsa loquitur* would only be applied where an injury raised an absolutely necessary inference that someone had been negligent. — (*Ronten v. McGehee*, 186 S.W. [2nd] 779, April 16, 1945, Arkansas.)

A somewhat different view of the doctrine was taken in a recent California case. The plaintiff was given a general anesthetic, and one of the defendants performed an appendectomy. When the plaintiff awoke he had a sharp pain in the right shoulder. After leaving the hospital this condition grew worse, he was unable to rotate his arm, and the arm became paralyzed and atrophied.

He brought suit against the doctor who had diagnosed his condition as appendicitis (the case is not clear whether this doctor was present at the operation), the doctor who performed the operation, the doctor who owned and operated the hospital, the anesthetist in the employ of the hospital and the special nurse who was in attendance after the operation.

The plaintiff introduced expert testimony to the effect that the paralysis was of traumatic origin. He then sought to invoke the doctrine of *res ipsa loquitur* to infer the defendants' negligence.

The trial court in entering a nonsuit as to all defendants found that there was no showing which defendant had control of the instrumentality causing the injury and that, since all defendants were not responsible for the acts of each other, the doctrine could not be applied. The plaintiff appealed and the judgment was reversed.

The court said that the unconscious patient is entitled to an explanation at least as much as the conscious pedestrian who is struck by an object coming from a building or other structure under the defendant's control. Concerning the relation of the various defendants, all of whom could hardly be held for a single act of negligence, the court found that all were temporary servants of the doctor performing the operation (*quere*) and that in any event the trial might absolve some of them from liability. Despite these difficulties the rule must be applied liberally so that those who were in a position to explain the injury are compelled to do so. Someone must in fact have been negligent and ought to be liable. The fact that the patient was unconscious and cannot identify the liable party does not deprive him of his rights. All the defendants were present for a common purpose.

The view taken here is that the doctrine applies because the defendants ought to have the burden

of going forward, since they are the ones in possession of the evidence. — (*Ybarra* v. *Spangard*, 154 Pac. [2d] 687, Dec. 27, 1944; rehearing denied Jan. 25, 1945, California.)

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR DECEMBER, 1945

RÉSUMÉ

Diseases	December 1945	December 1944	Seven-Year Median
Anterior poliomyelitis	11	11	6
Chancroid	2	5	*
Chicken pox	900	1407	1511
Diphtheria	20	29	20
Dog bite	426	517	550
Dysentery, bacillary	12	12	14
German measles	61	72	68
Gonorrhea	467	373	335
Granuloma inguinale	0	5	*
Lymphogranuloma venereum	0	2	*
Malaria	83	42	3
Measles	701	235	1082
Meningitis, meningococcal	13	26	11
Meningitis, Pfeiffer-bacillus	2	7	2
Meningitis, pneumococcal	1	9	6†
Meningitis, staphylococcal	1	0	0†
Meningitis, streptococcal	0	0	0†
Meningitis, other forms	3	1	2†
Meningitis, undetermined	2	1	2†
Mumps	669	1352	670
Pneumonia, lobar	165	232	396
Salmonella infections	5	5	5
Scarlet fever	523	1048	978
Syphilis	459	373	433
Tuberculosis, pulmonary	172	171	239
Tuberculosis, other forms	10	11	23
Typhoid fever	2	6	5
Undulant fever	10	3	3
Whooping cough	598	464	784

*Made reportable December, 1943.

†Four-year average.

COMMENT

Measles was reported less frequently during 1945 than during any year since 1907. During the month of December, however, there were three times as many cases as in December, 1944.

Scarlet fever was 50 per cent lower in December than it was during the corresponding month in 1944. In fact, from the months of August through December, 1945, the disease was reported less frequently than during a comparable period of months since 1940.

Cases of pneumonia were fewer than last year; in fact the number during December was lower than that for any December since reporting of pneumonia began in 1918.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Billerica, 1; Boston, 2; Concord, 1; Lowell, 1; Manchester, 1; Pittsfield, 1; Somerset, 1; Winthrop, 1; Worcester, 2; total, 11.

Anthrax was reported from: Franklin, 1; total, 1.

Diphtheria was reported from: Belmont, 1; Boston, 8; Franklin, 1; Hingham, 1; Lowell, 1; Millville, 1; Monterey, 1; Peabody, 1; Sudbury, 1; Taunton, 2; Tyngsboro, 1; Wayland, 1; total, 20.

Dysentery, amebic, was reported from: Camp Edwards, 1; Fort Devens, 1; Waltham Regional Hospital, 2; total, 4.

Dysentery, bacillary, was reported from: Boston, 2; Braintree, 2; Cambridge, 1; Chelsea, 1; Lowell, 1; Waltham, 2; Wrentham, 3; total, 12.

Malaria was reported from: Amherst, 1; Arlington, 1; Belmont, 1; Boston, 9; Brookline, 1; Cambridge, 1; Camp Edwards, 6; Chicopee, 1; Fort Devens, 31; Gloucester, 1; Hopedale, 1; Hull, 1; Lynn, 1; Medford, 1; Needham, 1; New Bedford, 1; Pittsfield, 1; Quincy, 1; Somerville, 2; Springfield, 1; Sutton, 1; Uxbridge, 1; Waltham, 1; Waltham Regional Hospital, 9; Wellesley, 1; Winthrop, 1; Worcester, 5; total, 83.

Meningitis, meningococcal, was reported from: Adams, 1; Arlington, 1; Boston, 3; Great Barrington, 1; Lowell, 2; Nahant, 1; Somerville, 1; Springfield, 1; Waltham Regional Hospital, 1; Watertown, 1; total, 13.

Meningitis, Pfeiffer-bacillus, was reported from: Arlington, 1; Methuen, 1; total, 2.

Meningitis, pneumococcal, was reported from: Worcester, 1; total, 1.

Meningitis, staphylococcal, was reported from: Wrentham (State School), 1; total, 1.

Meningitis, other forms, was reported from: Boston, 3; total, 3.

Meningitis, undetermined, was reported from: Cambridge, 1; Haverhill, 1; total, 2.

Salmonella infections were reported from: Cambridge, 1; Haverhill, 1; Malden, 1; North Andover, 1; Sheffield, 1; total, 5.

Septic sore throat was reported from: Attleboro, 4; Boston, 3; Cambridge, 2; Fall River, 1; Medford, 1; Merrimac, 1; Williamstown, 1; total, 13.

Trichinosis was reported from: Falmouth, 1; total, 1.

Typhoid fever was reported from: Boston, 1; Methuen, 1; total, 2.

Undulant fever was reported from: Adams, 1; Ashfield, 1; Brookline, 1; Fort Devens, 1; Hatfield, 1; North Andover, 2; Northampton, 1; Palmer, 1; Taunton, 1; total, 10.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Clinic Consultant
Lowell	February 1	Albert H. Brewster
Salem	February 4	Paul W. Hugenberger
Haverhill	February 6	William T. Green
Brockton	February 14	George W. Van Gorder
Worcester	February 15	John W. O'Meara
Pittsfield	February 18	Frank A. Slowick
Springfield	February 19	Garry deN. Hough, Jr.
Fall River	February 25	David S. Grice
Hyannis	February 26	Paul L. Norton

Physicians referring new patients to clinics should get in touch with the District Health Officer to make appointments.

MISCELLANY

CHANGES AT HARVARD SCHOOL OF PUBLIC HEALTH

Plans to increase the scope and importance of the Harvard School of Public Health were recently announced by President Conant. One of the world's foremost medical scientists, Brigadier General James Stevens Simmons, chief of the Preventive Medicine Service, Office of the Surgeon General, United States Army, has been appointed dean, succeeding Dr. Edward G. Huber, who has served as acting dean for the past several years. The Rockefeller Foundation has granted $1,000,000 for expenses of the school from July 1, 1946, to June 30, 1956, and Harvard University has set aside a sum of $750,000 to supplement the present endowment fund of the school.

In a reorganization intended to make this one of the outstanding research and teaching institutions in the world, the School of Public Health will have co-equal status with the Harvard Medical School and other professional divisions of the University. In addition to its present building at 55 Shattuck Street, Boston, the school will occupy the former Collis P. Huntington Memorial Hospital. Acquisition of this nearby hospital, which is to be remodeled, will give the school an additional 40,000 square feet of floor space.

SECTIONAL MEETINGS OF AMERICAN COLLEGE OF SURGEONS

The American College of Surgeons announces the resumption in 1946 of its sectional meetings, which during the war were replaced by one-day war sessions. Ten two-day meetings are planned, to begin in Minneapolis, with headquarters at the Radisson Hotel, on January 28 and 29. The second meeting will be held in the Hotel Jefferson, St. Louis, on January 31 and February 1; the third at the Tutwiler Hotel, Birmingham, on February 8 and 9; the fourth in the William Penn Hotel, Pittsburgh, on March 11 and 12; the fifth at The Copley-Plaza, Boston, on March 18 and 19; the sixth in the

Mount Royal Hotel, Montreal, on March 22 and 23; the seventh at the Statler Hotel, Detroit, on March 26 and 27; the eighth in the Utah Hotel, Salt Lake City, on April 8 and 9; the ninth at the Multnomah Hotel, Portland, Oregon, on April 12 and 13; and the last in the Biltmore Hotel, Los Angeles, on April 17 and 18.

The medical profession at large, medical students and hospital executives are invited to join with the fellows of the College in these meetings. The invitation has been extended to the entire medical and hospital profession because only local meetings of medical groups have been held during the past three or four years and the College recognizes the need for disseminating information about new methods and therapies through larger meetings addressed by nationally prominent speakers.

CORRESPONDENCE

A CORRECTION

To the Editor: In the July 12, 1945, issue of your journal, an item was published relating to a court case in Vermont where a decision was rendered involving a man by the name of Haskins, where suit had been brought for compensation for Christian Science treatment.

I believe it is only just to you and your readers to know that Haskins was never listed as a Christian Science practitioner in *The Christian Science Journal*, which is the organ of the Christian Science church containing a list of those who have the necessary qualifications to be recognized as authorized practitioners by The Christian Science Board of Directors. Although he was at one time a member of the Christian Science church, he is no longer a member.

It is true, as stated in your report, that "it is a violation of the rules of the church for a Christian Science practitioner to bring suit at law to recover for treatments given to a patient."

Wm. D. Kilpatrick
Manager of Committees on Publication

The First Church of Christ, Scientist
107 Falmouth Street
Boston 15

NOTICES

ANNOUNCEMENTS

Dr. Leo Alexander announces his return from service in the United States Army and the opening of his office at 433 Marlborough Street, Boston, for the practice of psychiatry and neurology.

Dr. Joseph G. Cutler, having returned from overseas duty with the United States Army, announces the opening of his office at 397 Essex Street, Salem, for the practice of pediatrics.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.
Medical Conference Program

Friday, February 1. Diseases of the Orbit. Dr. Benjamin Sachs.

Wednesday, February 6 — Obstetric Trends during the Last Five Years. Dr. Alonzo K. Paine.

Friday, February 8 — Physiologic Evaluation of Quartermaster Clothing and Equipment. Colonel John H. Talbot.

Wednesday, February 13 — The Treatment of Laennec Cirrhosis. Dr. Roy C. Crosby.

Friday, February 15 — Diagnosis of Congenital Heart Disease by Venous Catheterization. Dr. Lewis Dexter.

Wednesday, February 20 — Psychologic Aspects of the Menstrual Cycle. Dr. Norris T. Flanagan.

Friday, February 22 — Holiday.

Wednesday, February 27 — Practical Aspects of Ringworm Diseases. Dr. Ernst Bernhardt.

On Tuesday and Thursday mornings, Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr. William Dameshek.

All morning conferences are open to the medical profession.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, February 7, in the classroom of the Nurses' Residence at 7:15 p.m. Dr. Siegfried Thannhauser will discuss an interesting case of jaundice. Dr. Helena M. Murphy will be chairman.

UROLOGY AWARD

The American Urological Association offers an annual award, not to exceed $500, for an essay (or essays) on the result of some specific clinical or laboratory research in urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deems none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write the secretary for full particulars. The selected essay (or essays) will appear on the program of the meeting of the American Urological Association to be held at the Netherland Plaza, Cincinnati, July 22 to 25. All essays must be in the hands of the secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee, on or before July 1.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, January 31

Friday, February 1
- *9:00–10:00 a.m. Medical clinic. Isolation Amphitheater, Children's Hospital.
- *9:00–10:00 a.m. Diseases of the Orbit. Dr. Benjamin Sachs. Joseph H. Pratt Diagnostic Hospital.
- *10:00 a.m.–12:00 m. Medical staff rounds. Peter Bent Brigham Hospital.
- 10:50 a.m. Postgraduate clinic in dermatology and syphilology. Amphitheater, Dowling Building, Boston City Hospital.

Monday, February 4
- *12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

Tuesday, February 5
- *9:00–10:00 a.m. Medical clinic. Infants' Hospital.
- *12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

Wednesday, February 6
- *9:00–10:00 a.m. Obstetric Trends during the Last Five Years. Dr. Alonzo K. Paine. Joseph H. Pratt Diagnostic Hospital.
- *12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

January 7–April 22, 1946. Metropolitan State Hospital. Eleventh postgraduate seminar in neurology and psychiatry. Page 314, issue of September 6.

January 30. Arlington Doctors Club and Belmont Medical Club. 8.00 p.m. Ring Sanatorium and Hospital.

February 1–27. Joseph H. Pratt Diagnostic Hospital. Medical conference program. Notice above.

February 2. American Board of Obstetrics and Gynecology. Page 514, issue of October 25.

February 4–March 29. Health Education Institute. Page 746, issue of December 13.

February 7. New England Hospital for Women and Children. Notice above.

February 9. New England Dermatological Society. Page xix, issue of January 17.

February 13. Massachusetts Medico-Legal Society. Page xix, issue of January 17.

February 14. Diagnostic and Therapeutic Suggestions in Cardiovascular Disease. Dr. John Sproull. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

February 20. Tufts Medical Alumni Lecture. Page xix, issue of January 17.

May 13–17. American College of Physicians. Page 798, issue of December 20.

District Medical Society

WORCESTER

February 13. Worcester State Hospital.
March 13. Worcester Memorial Hospital.
April 10. Hahnemann Hospital.
May 8. Annual meeting.